Supporting Information

Discovery, Synthesis and Biological Evaluation of a Novel Group of Selective Inhibitors of Filoviral Entry

Maria V. Yermolina,[†] *Jizhen Wang,*[‡] *Michael Caffrey*[$$] *Lijun L. Rong,*[‡] *and Duncan J. Wardrop.*[*,†]

[†]Department of Chemistry, University of Illinois, 845 West Taylor Street, Chicago, Illinois 60607.

[$$]Department of Biochemistry and Molecular Genetics, University of Illinois at Chicago, 900 South Ashland, Chicago, IL 60607

[‡] Department of Microbiology & Immunology, University of Illinois at Chicago, 835 South Wolcott, Chicago, Illinois 60612

wardropd@uic.edu

*To whom correspondence should be addressed

Phone: 312-355-1035. Fax: 312-996-0431. Email: wardropd@uic.edu.

† Department of Chemistry, University of Illinois at Chicago.

‡ Microbiology & Immunology, University of Illinois at Chicago.

Table of Contents

Schematic representation of production of GP-pseudotyped HIV virions and luciferase assay S2

^{1}H and ^{13}C spectral data for all new compounds S3-S60

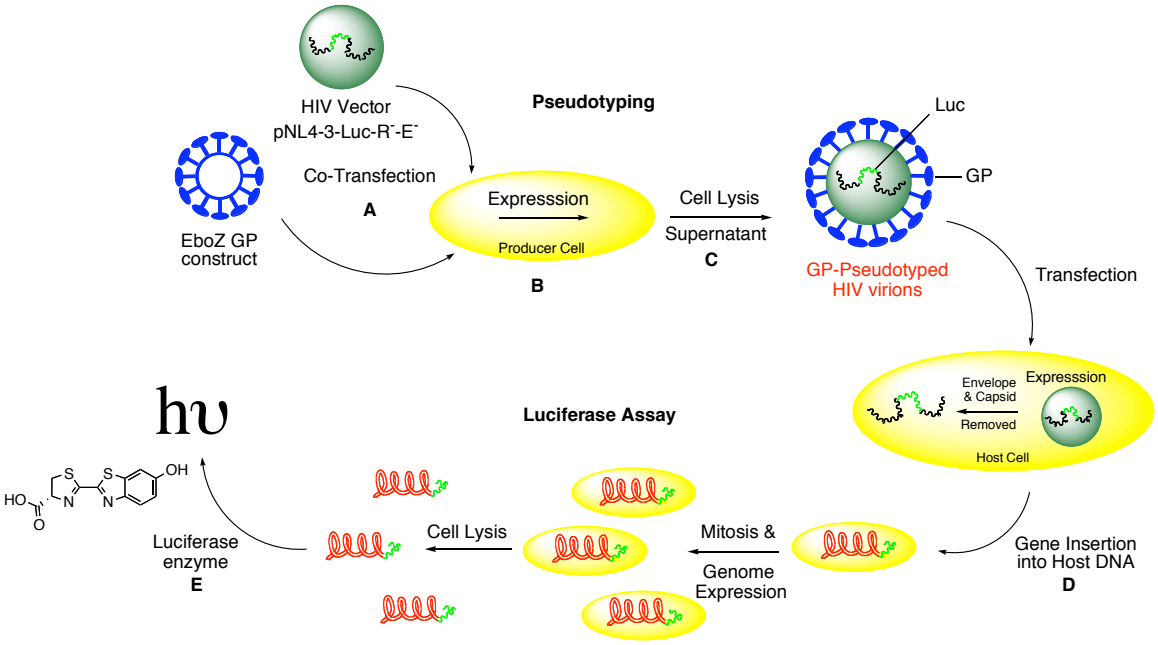
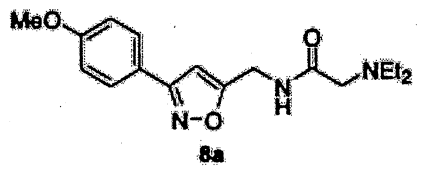
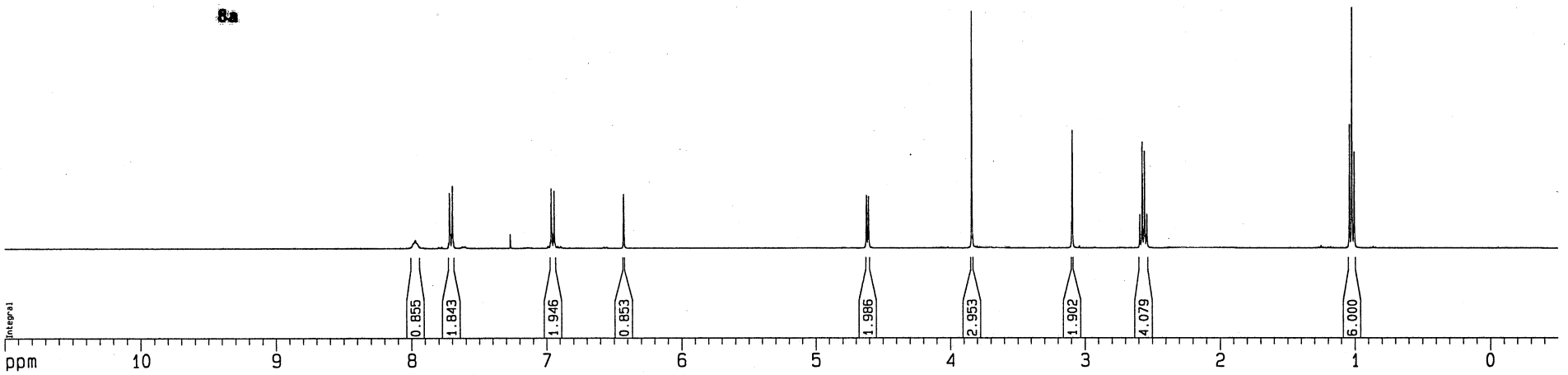
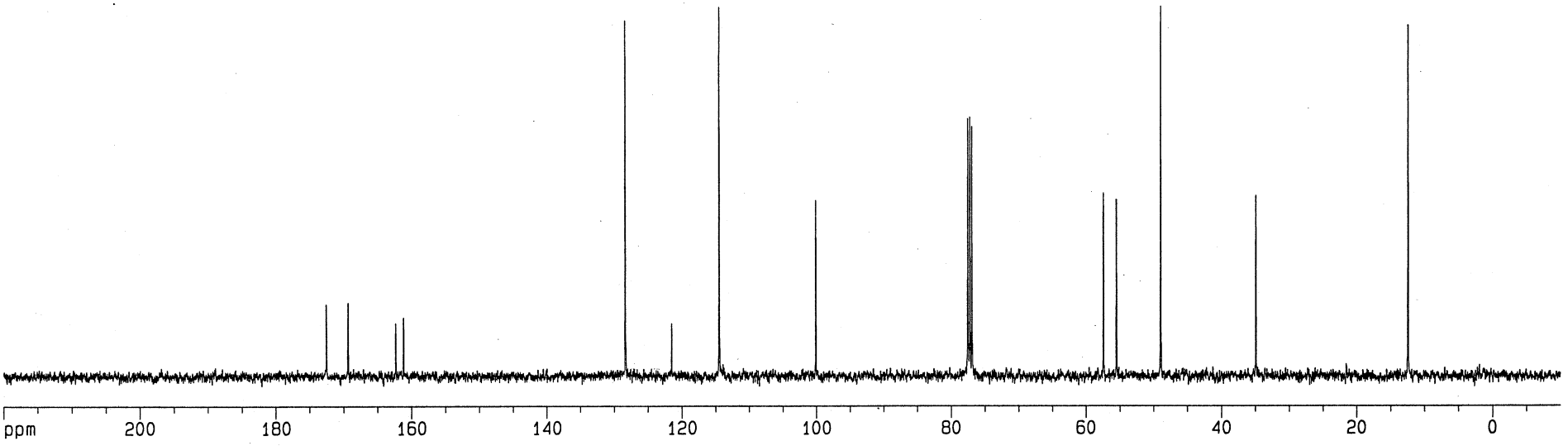


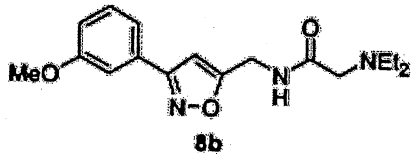
Figure S1. Schematic representation of the production of GP-pseudotyped HIV virion followed by luciferase protocol. (**A**). To produce HIV-GP pseudotyped virions, 293T cells were co-transfected with HIV vector pHL4-3 (HIV genome containing a luciferase reporter gene (pNL4-3-Luc-R--E-, green)) and EboZ GP construct. HIV vector carries a deletion within the *env* coding region and harbores a reporter gene to be transferred to the target cells. It also contains all sequences necessary for reverse transcription, vector integration, and expression other reporter gene. (**B**). Upon transfection of cells an envelope deficient HIV virus vector and a plasmid encoding EboZ virus envelope are coated and expressed in producer cells generating exclusively the GP pseudotyped HIV virions. (**C**). The last are assembled, released upon cell lyses, and collected. Lusiferase Assay. (**D**). To examine incorporation of HIV-GP pseudotyped virus into 293T it transfects into the host cells so desired genome is expressed. Recombinant pseudotyped virus carried the recombinant genome is produced and replicated through mitoses. (**E**). The luciferase gene is expressed releasing luciferase enzyme upon cell lyses. The total GP expression (enzyme activity) level is detected by luciferse assay protocol using Western blotting.


MeO
O
NEt2
N
H
N-O

8a

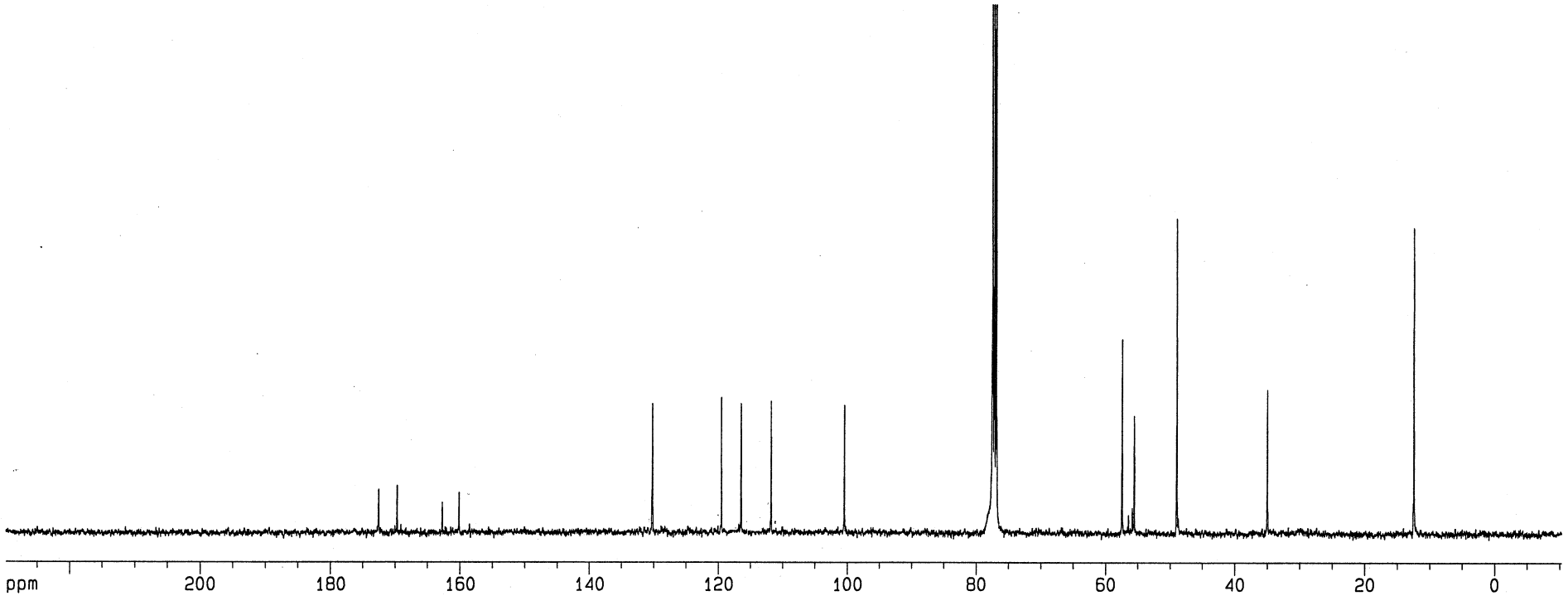

Integral
0.855
1.843
1.946
0.853
1.986
2.953
1.902
4.079
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

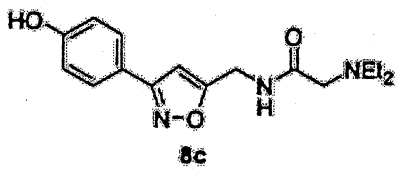

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
N-O
N
H
O
NEt2

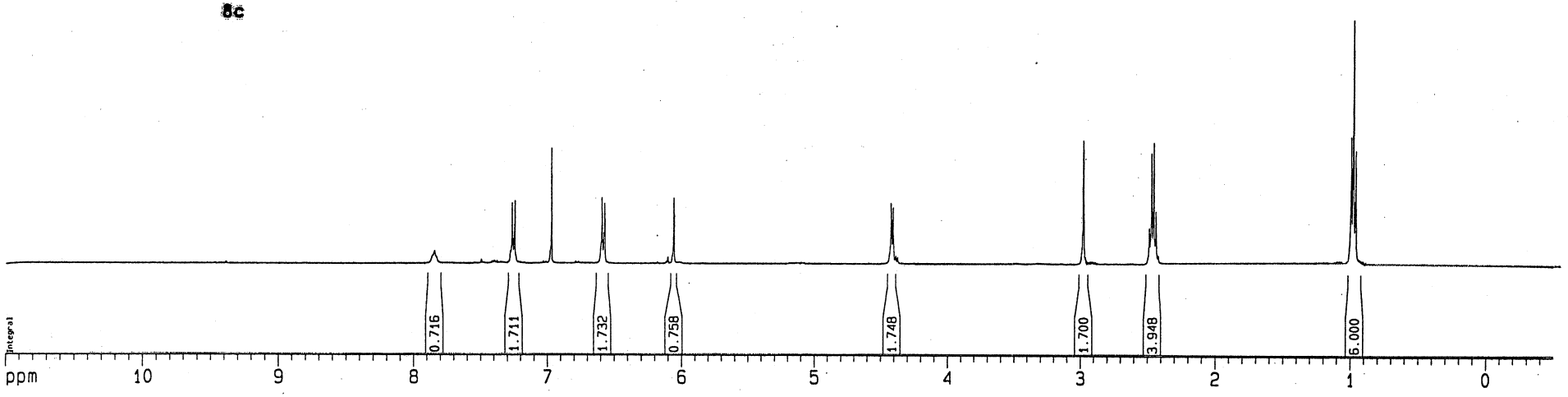
8b

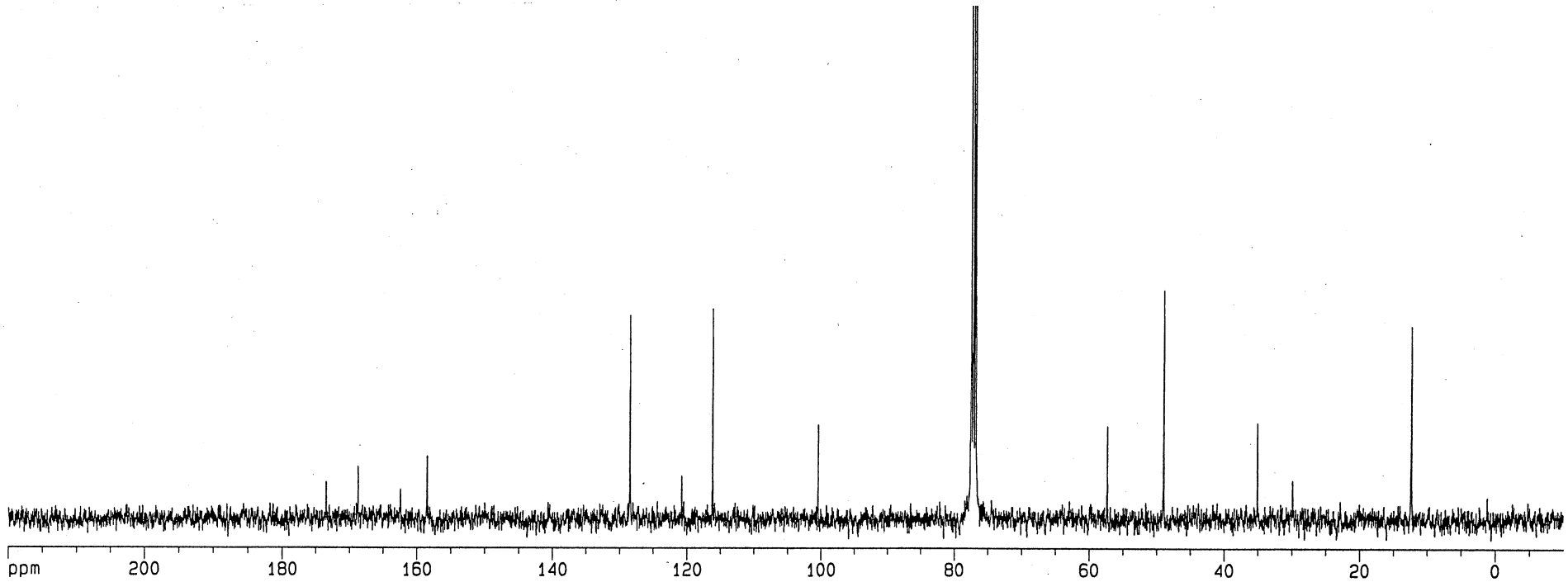
Integral
0.644
1.609
0.522
0.569
1.392
2.913
1.510
3.429
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

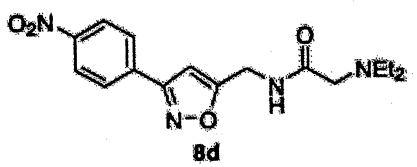

ppm
200
180
160
140
120
100
80
60
40
20
0


HO
O
NEt2
N
H
N-O

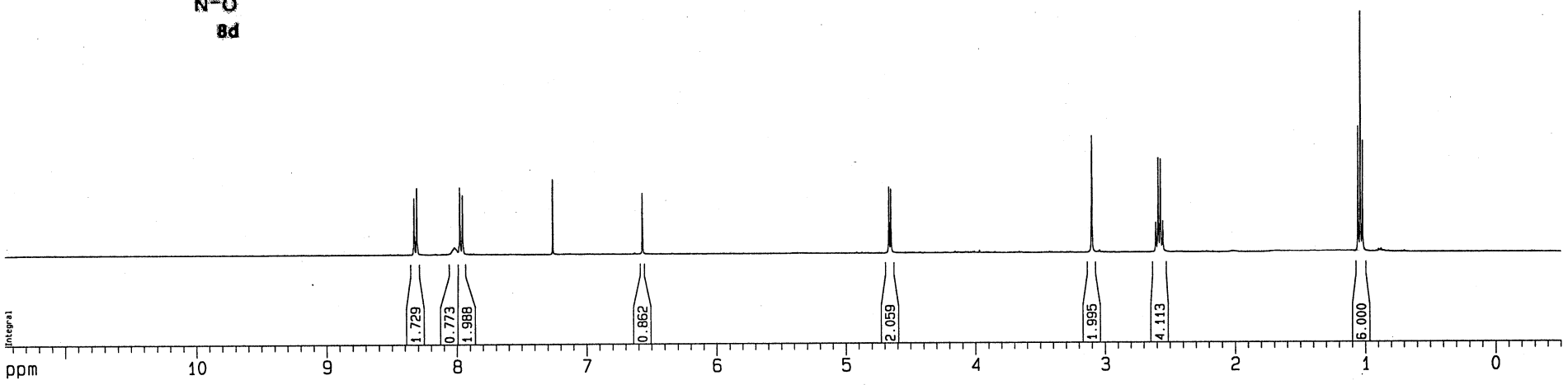
8c

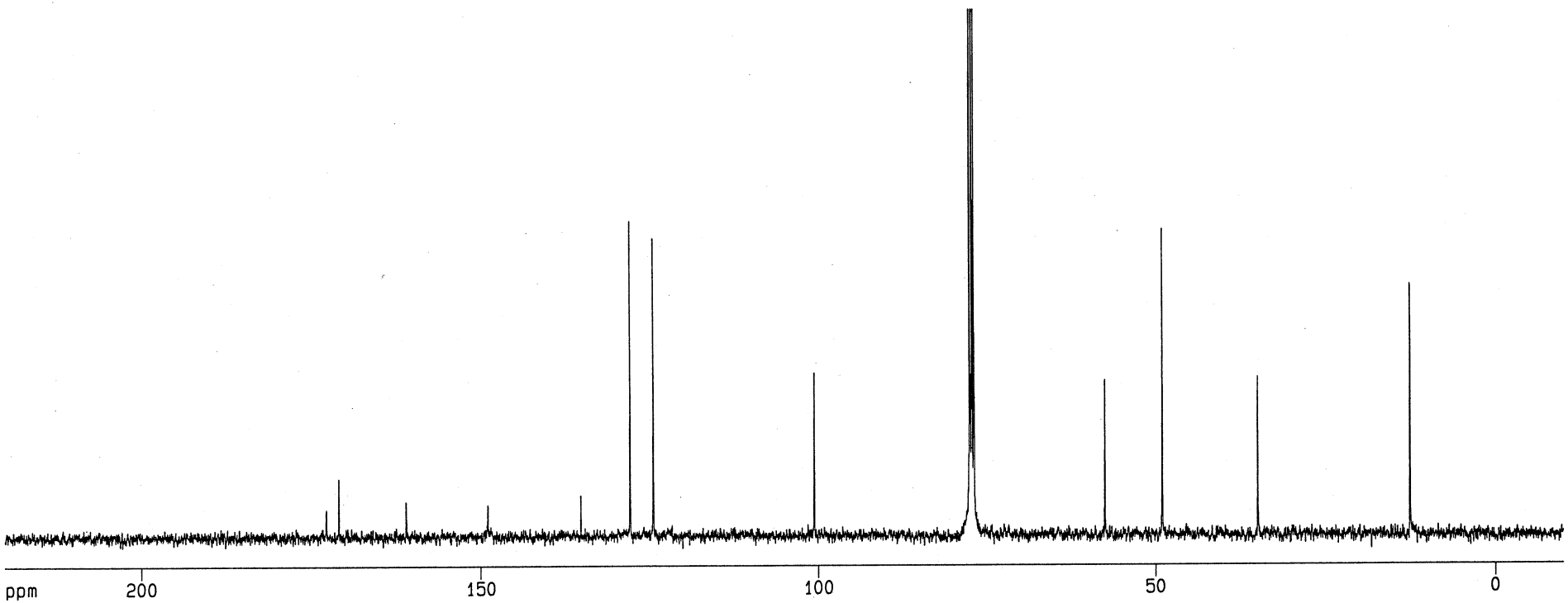

Integral
0.716
1.711
1.732
0.758
1.748
1.700
3.948
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

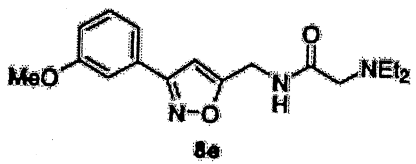

ppm
200
180
160
140
120
100
80
60
40
20
0


O2N
O
NEt2
N
H
N–O

8d

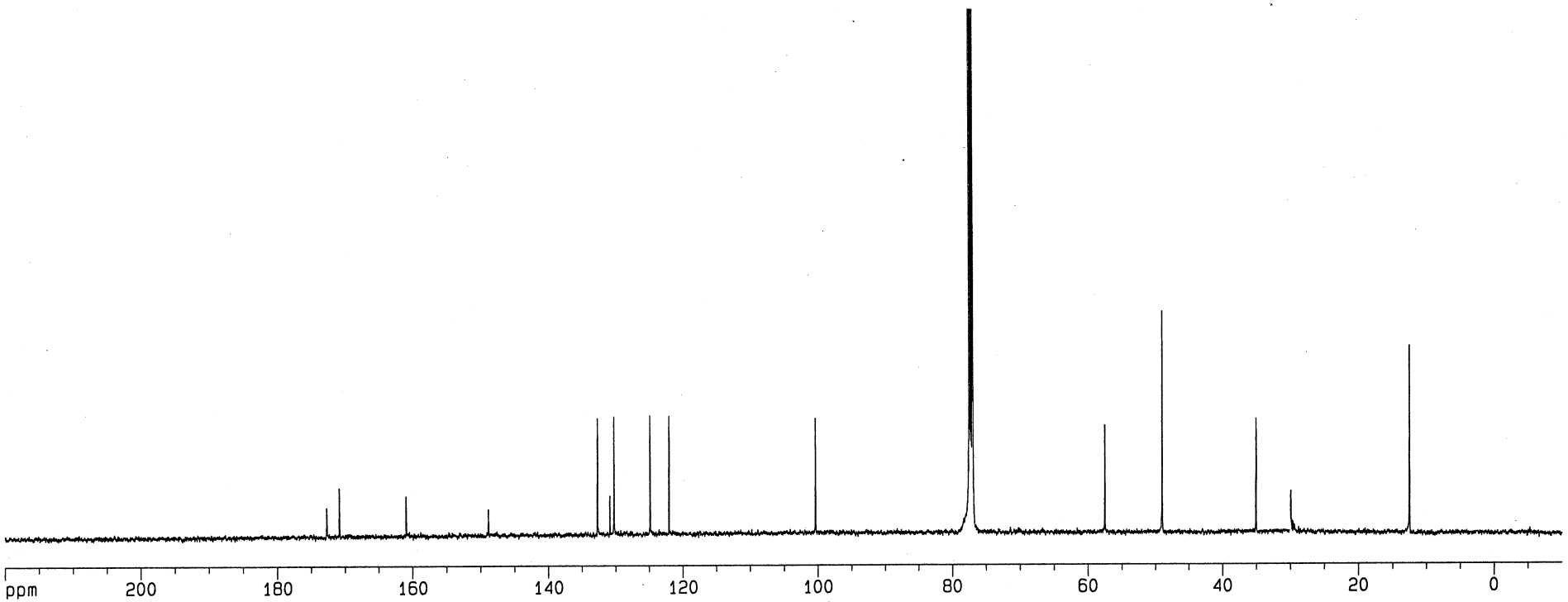

Integral
1.729
0.773
1.988
0.862
2.059
1.995
4.113
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

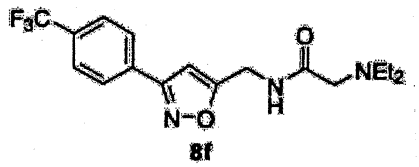

ppm
200
150
100
50
0


MeO
O
NEt2
N
H
N–O

8e

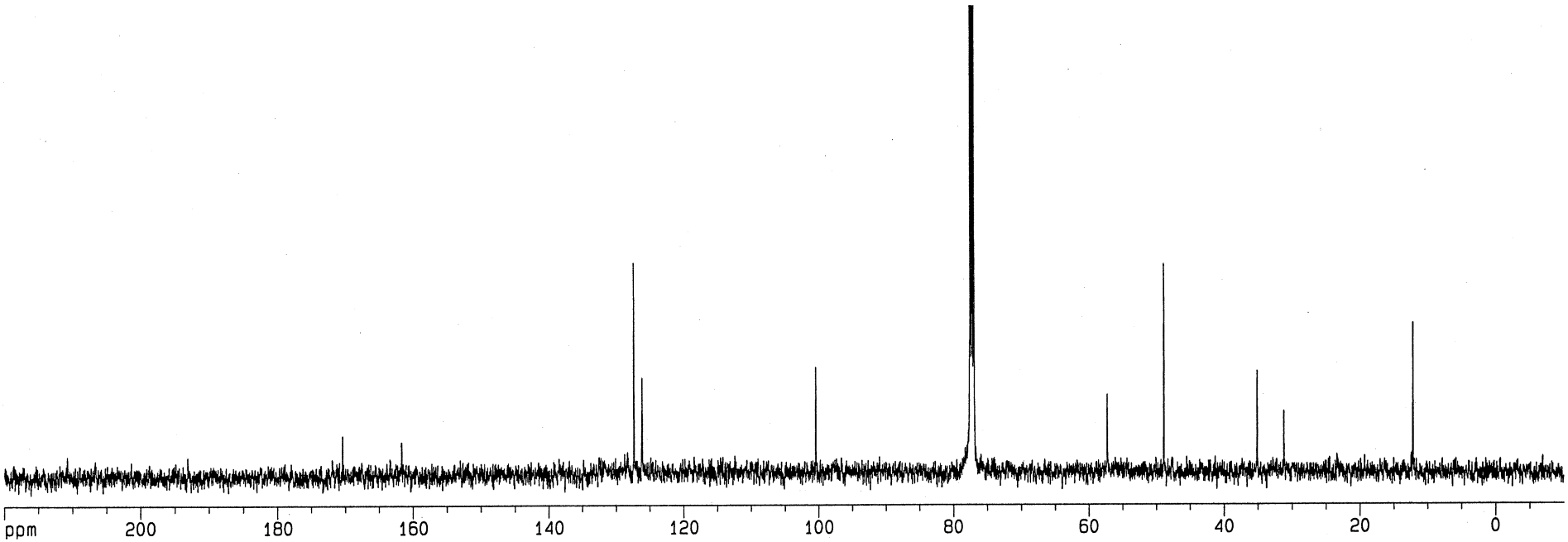
Integral
0.812
0.830
0.914
0.790
0.946
0.850
1.808
1.750
3.989
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

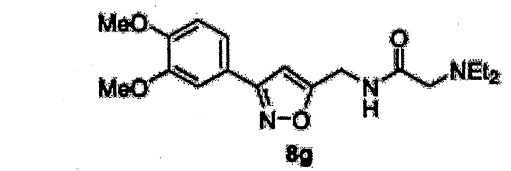

ppm
200
180
160
140
120
100
80
60
40
20
0


F3C
O
NEt2
N
H
N-O

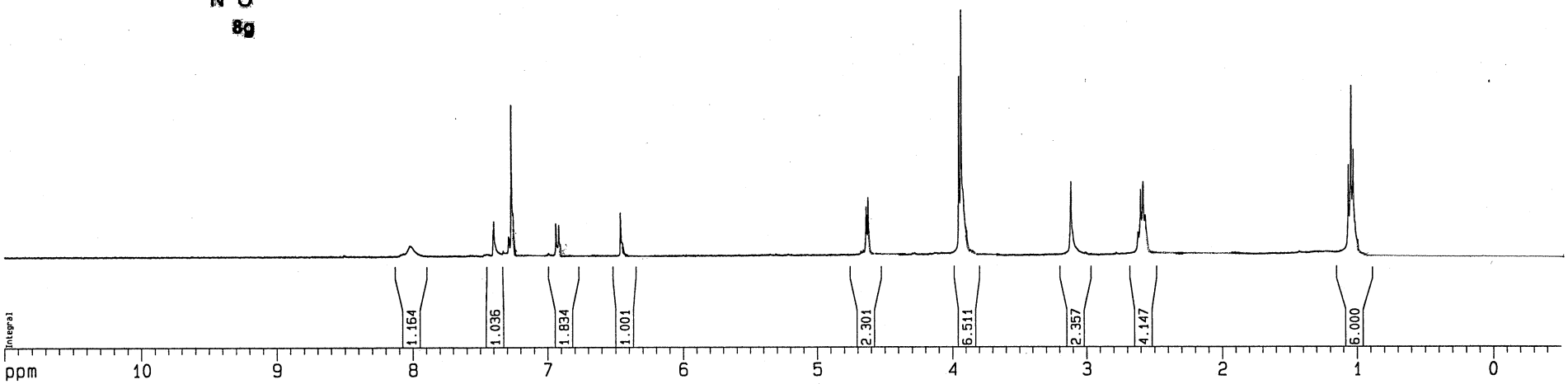
8f

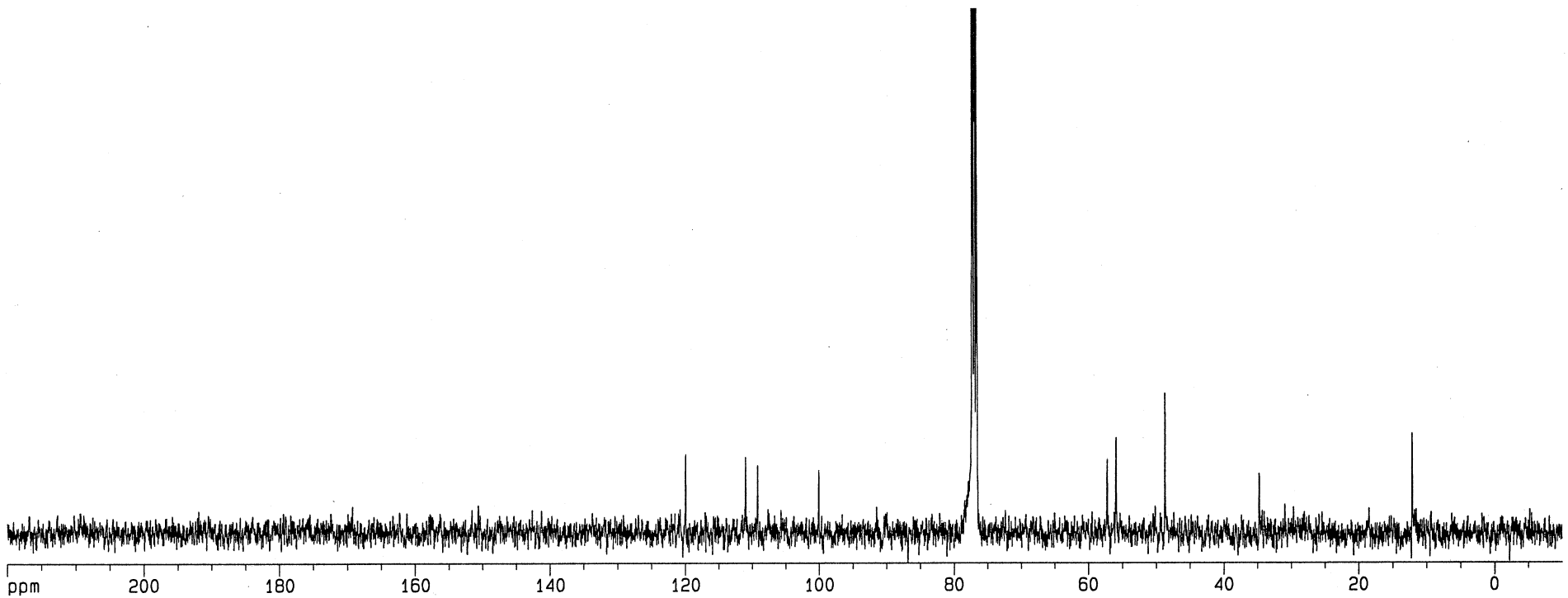
Integral
0.934
2.120
2.165
0.968
2.017
2.017
4.383
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

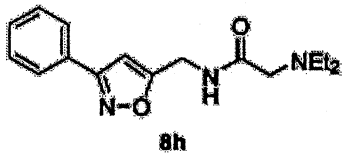

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
MeO
N–O
N
H
O
NEt2

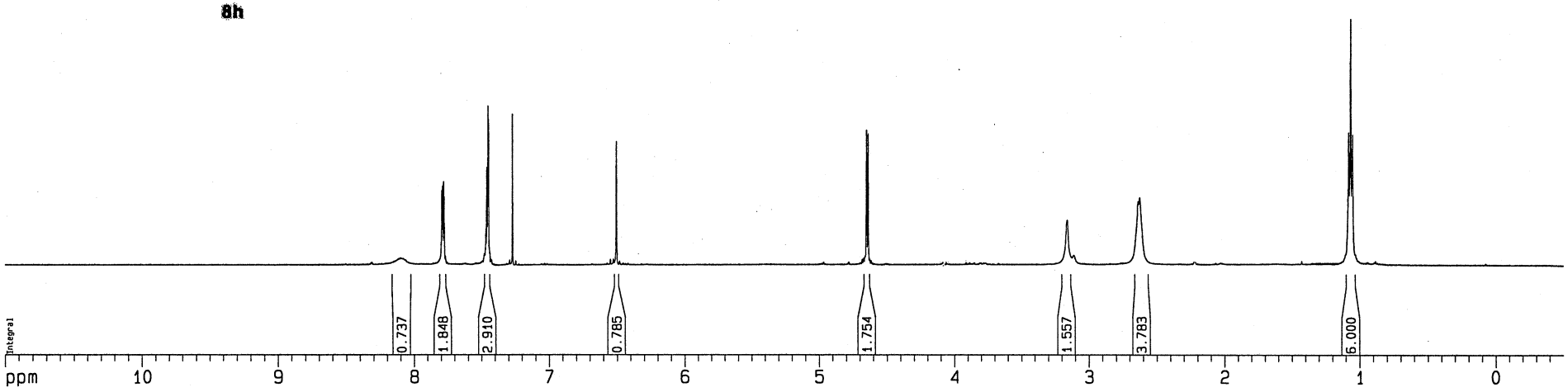
8g

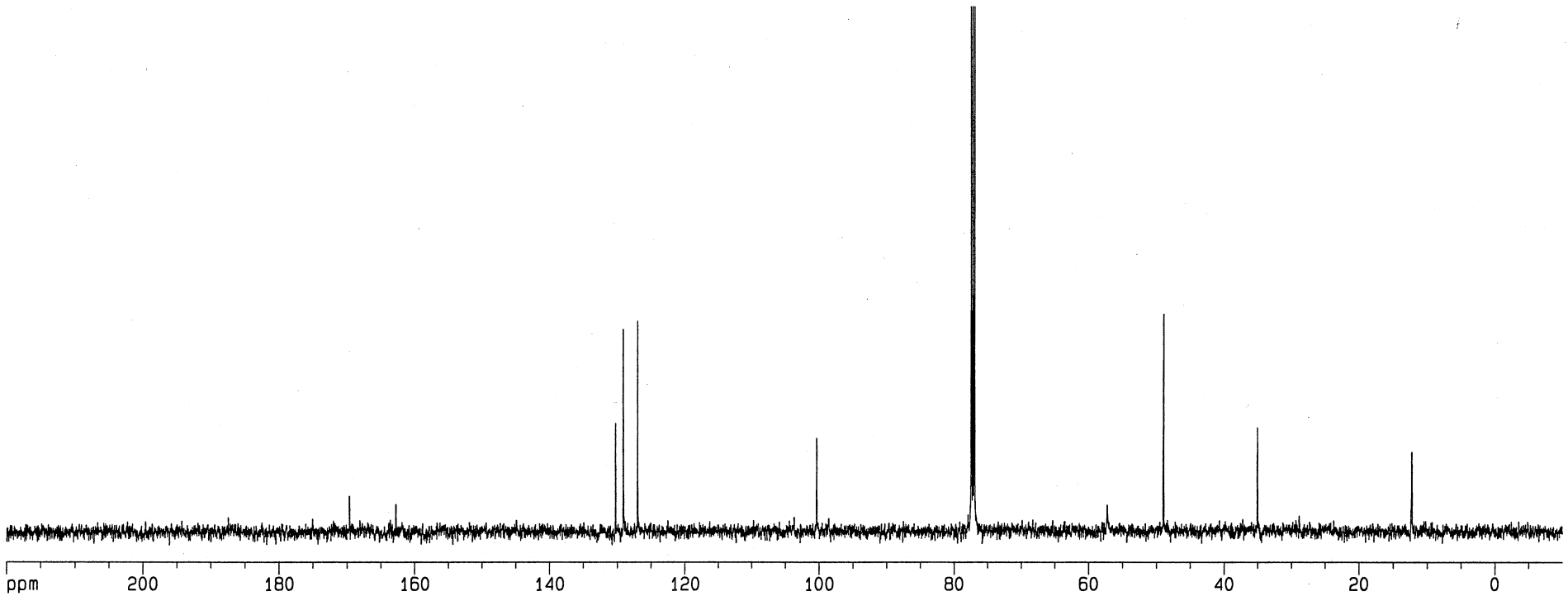

Integral
1.164
1.036
1.834
1.001
2.301
6.511
2.357
4.147
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

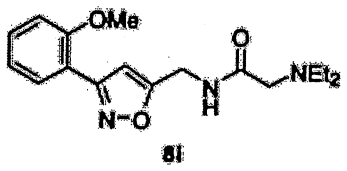

ppm
200
180
160
140
120
100
80
60
40
20
0


O
NEt2
N
H
N-O

8h

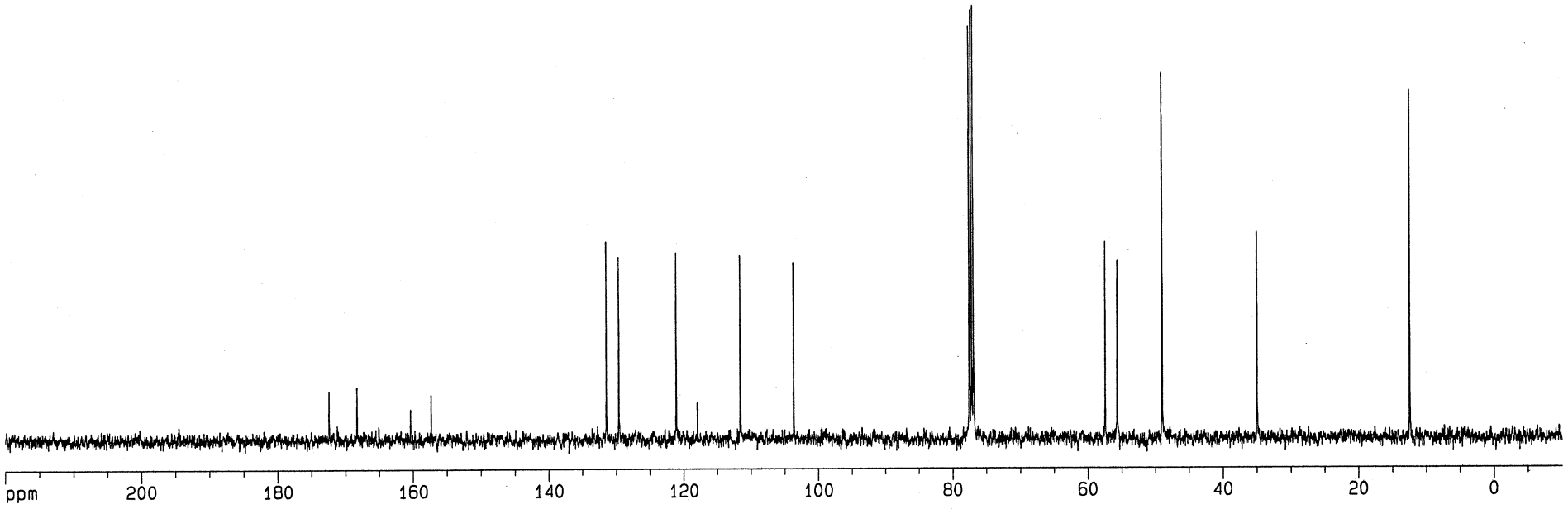

Integral
0.737
1.848
2.910
0.785
1.754
1.557
3.783
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

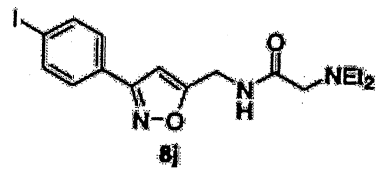

ppm
200
180
160
140
120
100
80
60
40
20
0


OMe
O
NEt2
N
H
N-O

8i

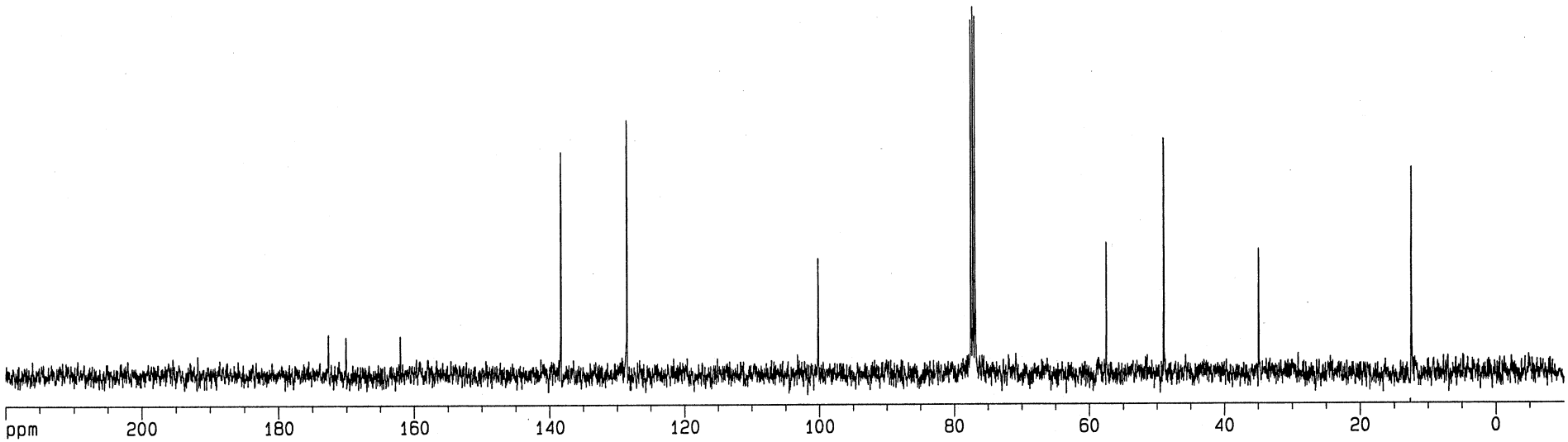
Integral
0.745
0.865
0.897
2.008
0.767
1.803
2.856
1.788
4.071
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

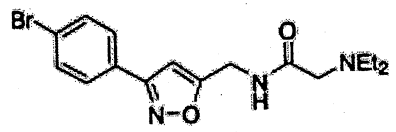

ppm
200
180
160
140
120
100
80
60
40
20
0


I
O
NEt2
N
H
N-O

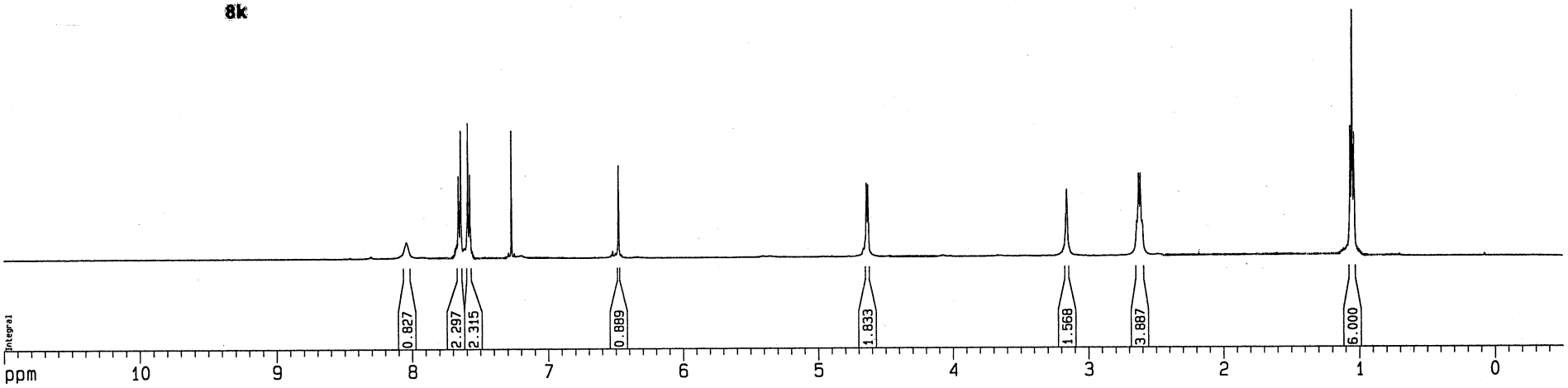
8j

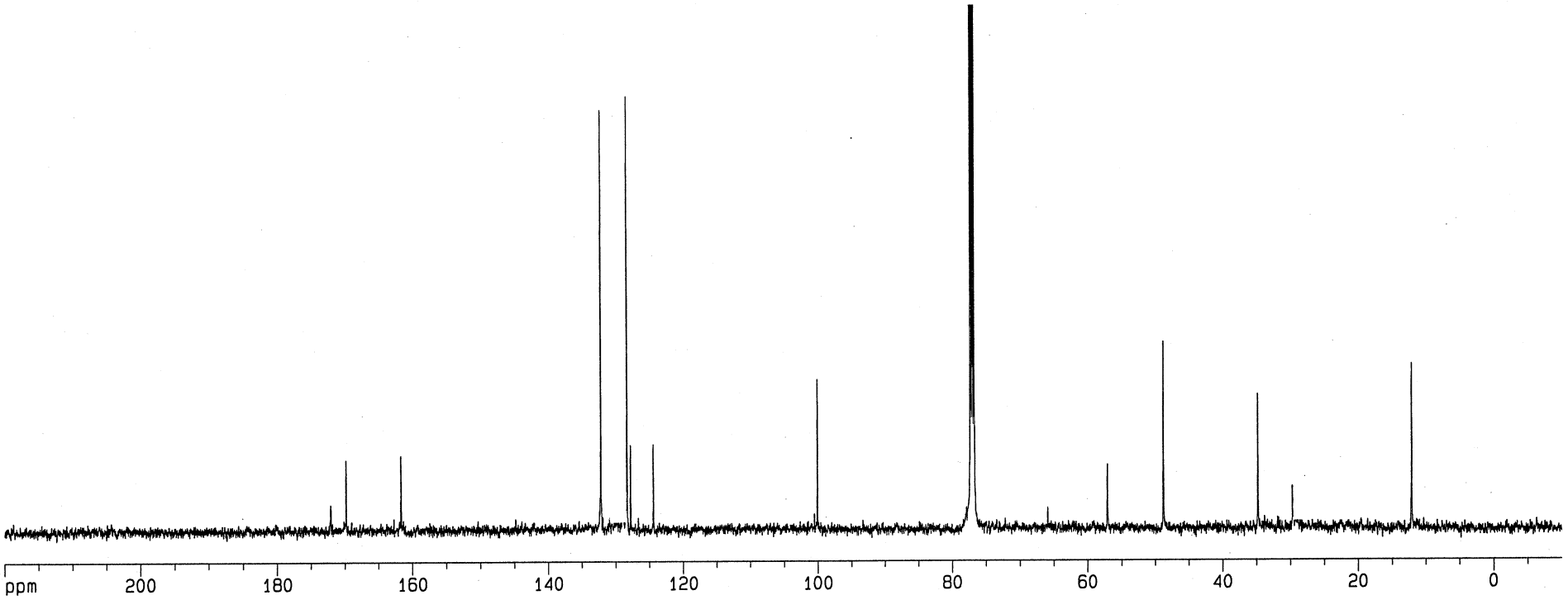
Integral
0.827
1.648
1.755
0.546
1.783
1.070
4.123
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

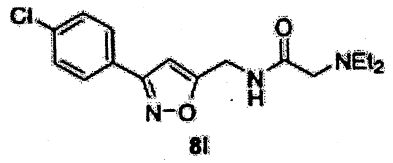

ppm
200
180
160
140
120
100
80
60
40
20
0


Br
O
NEt2
N
H
N–O

8k

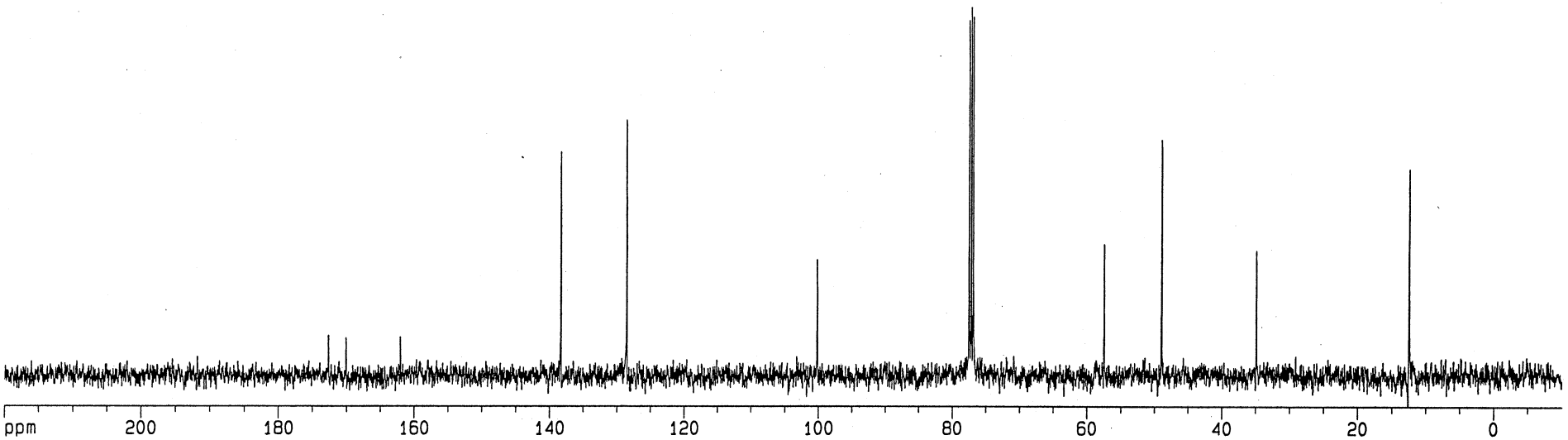

Integral
0.827
2.297
2.315
0.889
1.833
1.568
3.887
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

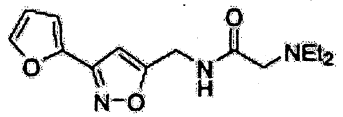

ppm
200
180
160
140
120
100
80
60
40
20
0


Cl
O
NEt2
N
H
N–O

8l

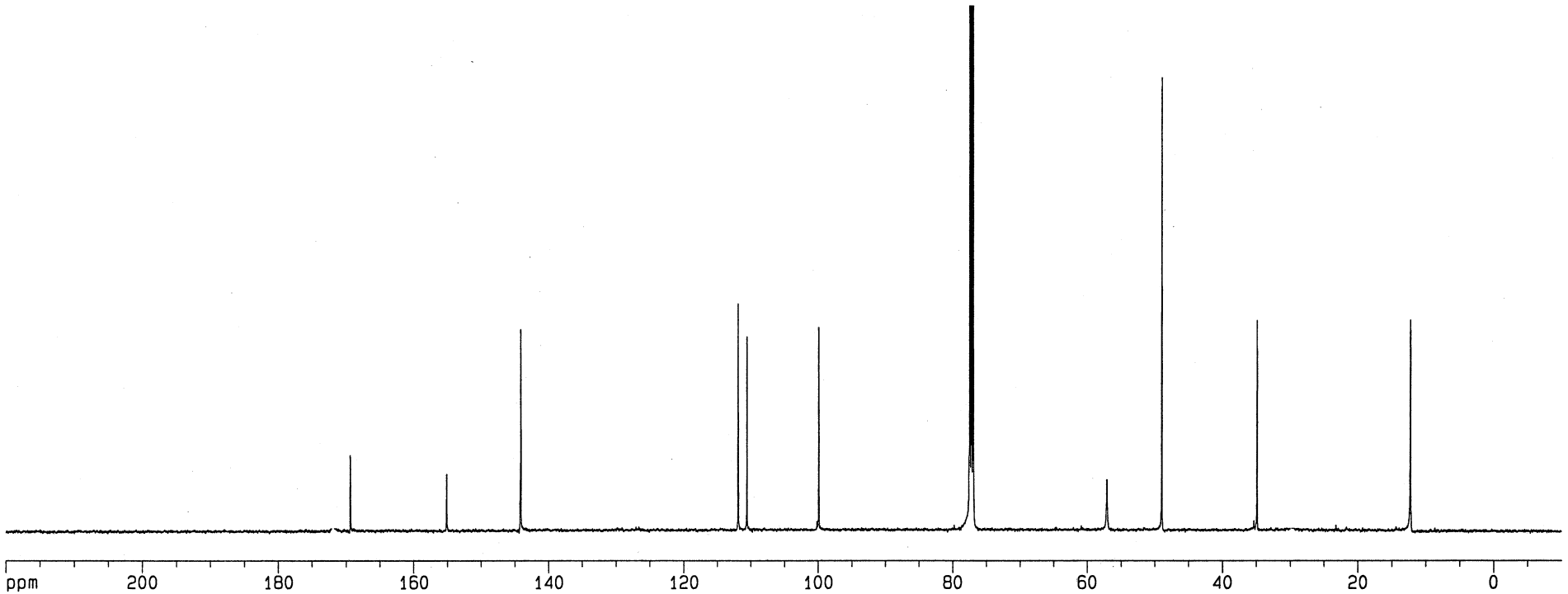
Integral
0.827
1.648
1.755
0.546
1.783
1.070
4.123
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

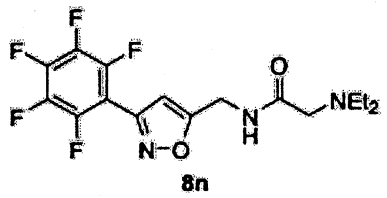

ppm
200
180
160
140
120
100
80
60
40
20
0


O
NEt2
N
H
N–O
O

8m

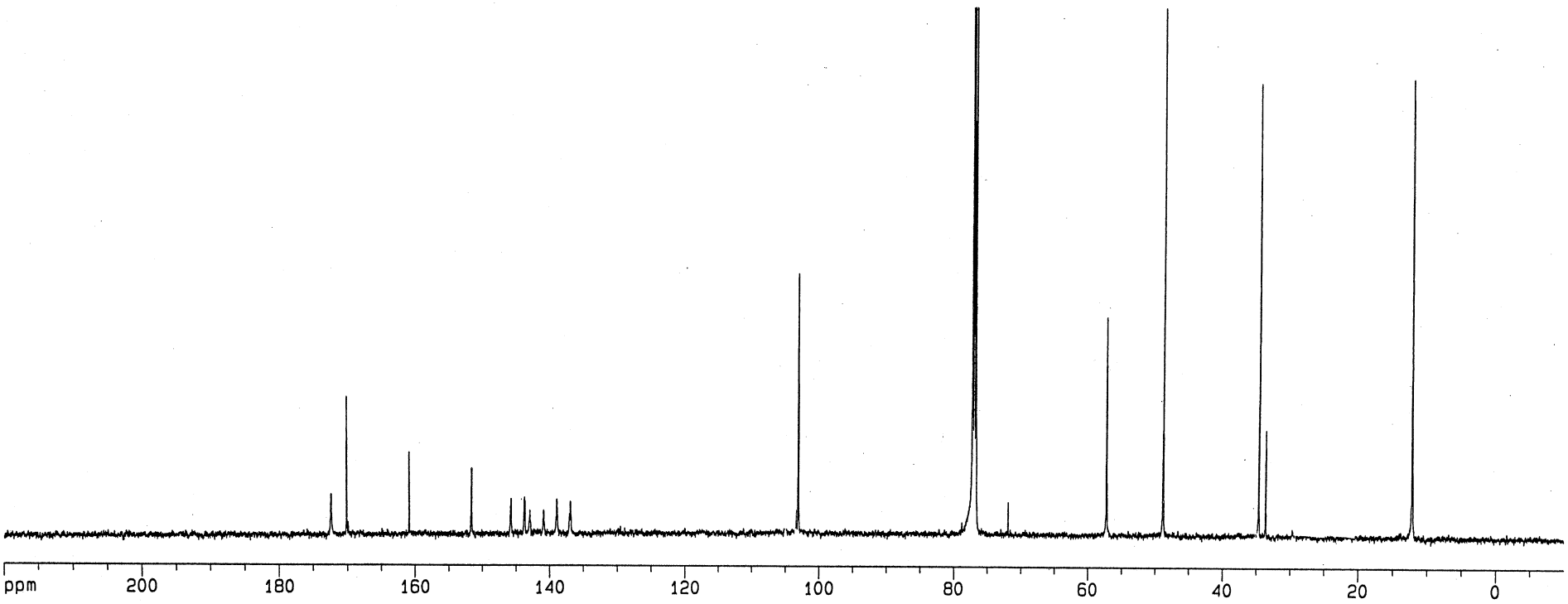
Integral
0.636
0.802
0.795
0.833
0.807
1.932
1.588
3.755
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

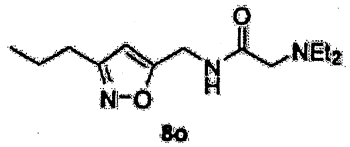

ppm
200
180
160
140
120
100
80
60
40
20
0


F
F
F
F
F
N–O
O
N
H
NEt2

8n

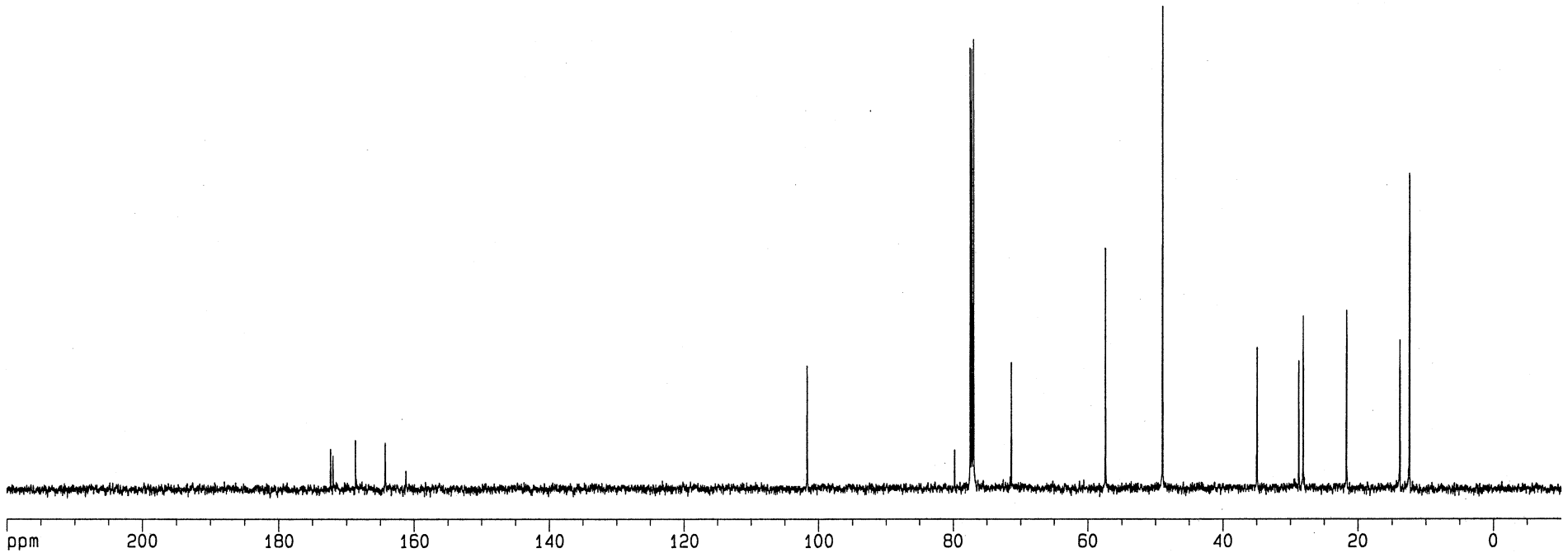
Integral
0.873
0.929
1.992
1.720
3.863
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

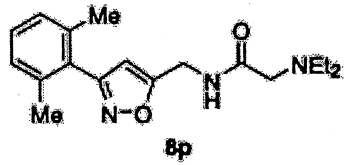

ppm
200
180
160
140
120
100
80
60
40
20
0


O
NEt2
N
H
N-O

8o

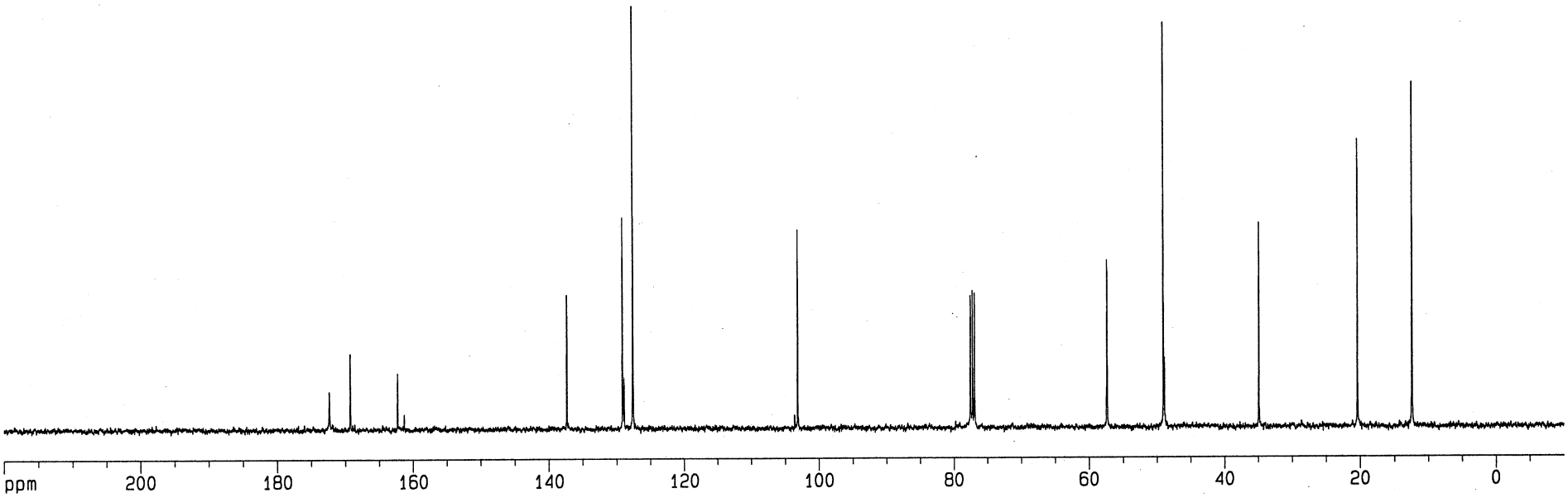
Integral
0.622
0.819
2.011
1.955
4.155
2.179
6.374
3.000
ppm
10
9
8
7
6
5
4
3
2
1
0

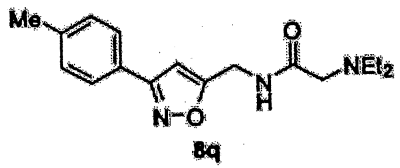

ppm
200
180
160
140
120
100
80
60
40
20
0


Me
O
NEt2
N
H
Me
N–O

8p

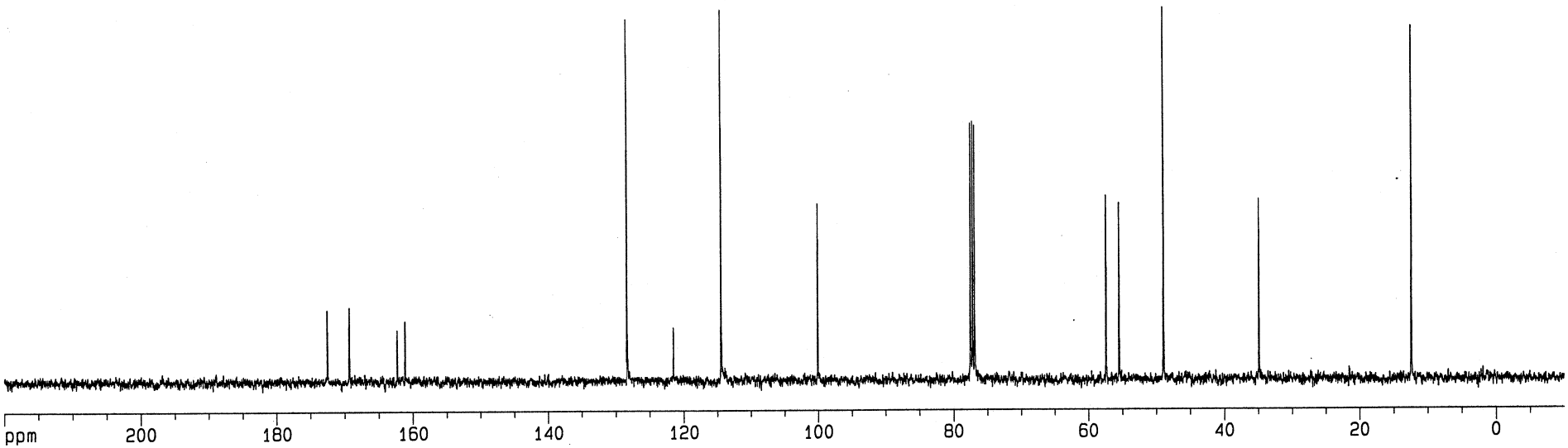
Integral
0.706
0.841
1.708
0.704
1.706
1.721
4.068
5.418
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

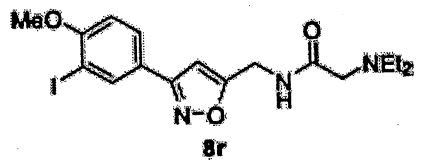

ppm
200
180
160
140
120
100
80
60
40
20
0


Me
O
NEt2
N
H
N
O

8q

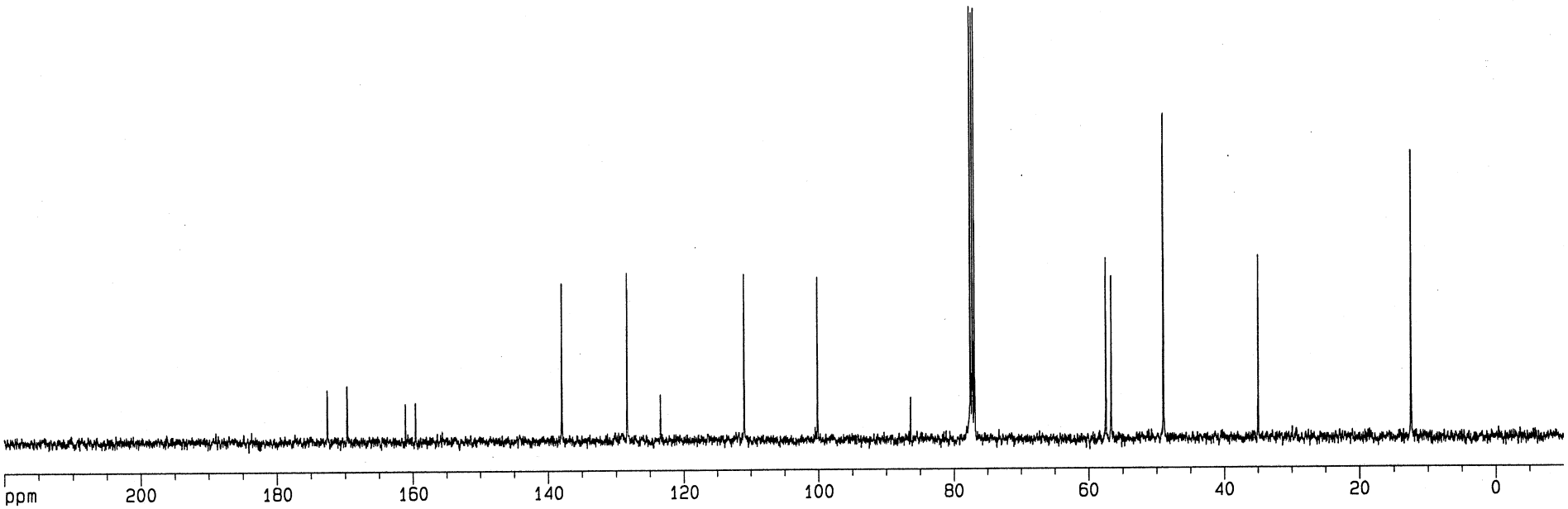
Integral
0.844
1.821
1.919
0.889
1.995
1.947
4.000
2.688
5.948
ppm
10
9
8
7
6
5
4
3
2
1
0

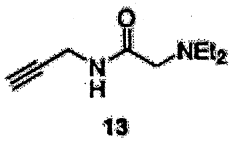

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
I
N-O
O
NEt2
N
H

8r

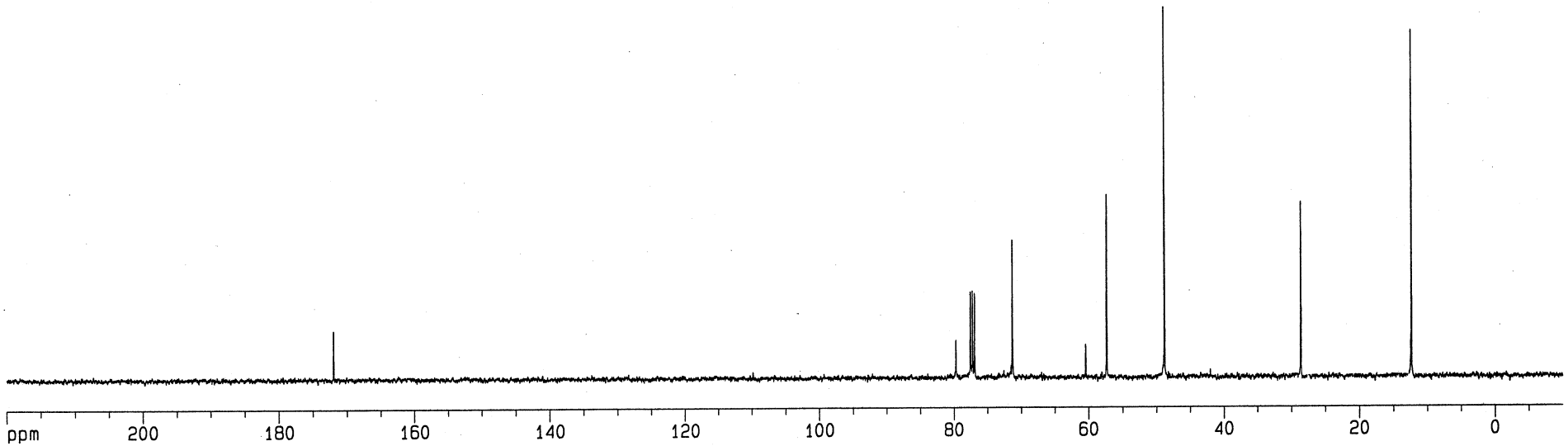
Integral
0.797
0.880
0.905
0.937
0.877
1.996
2.864
1.990
4.064
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

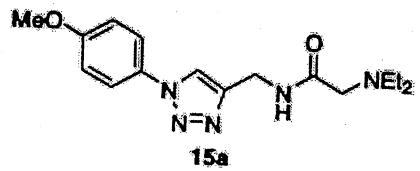

ppm
200
180
160
140
120
100
80
60
40
20
0


O
N
H
NEt2

13

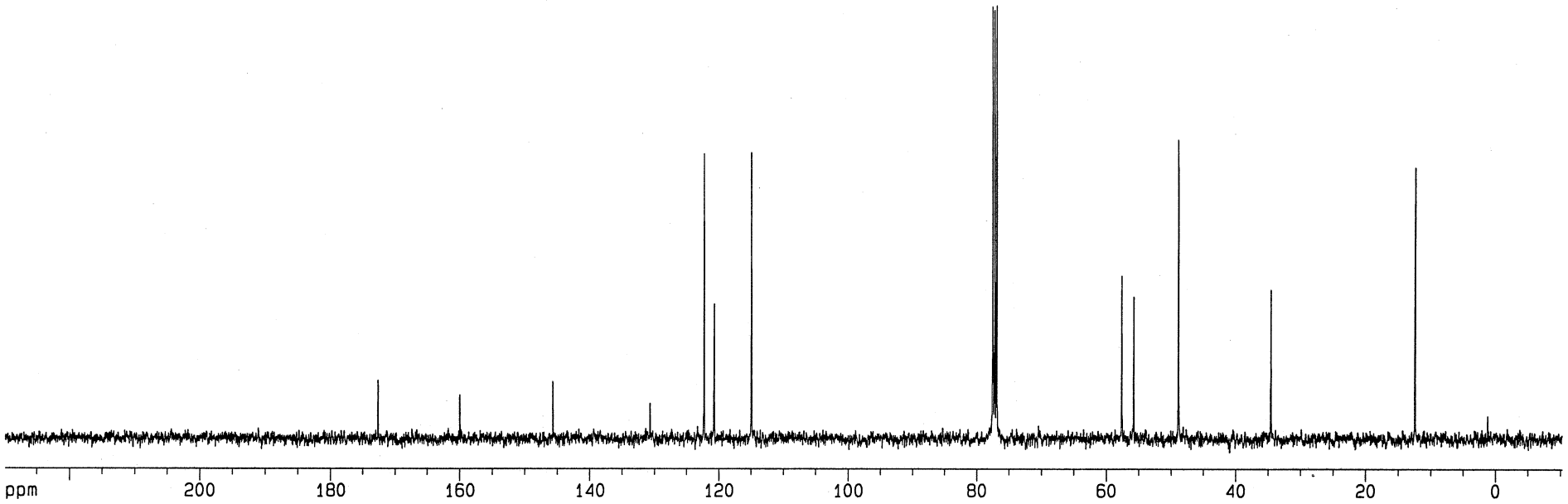
Integral
0.756
2.000
1.918
4.093
0.853
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

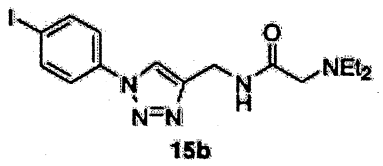

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
N
N=N
N
H
O
NEt2

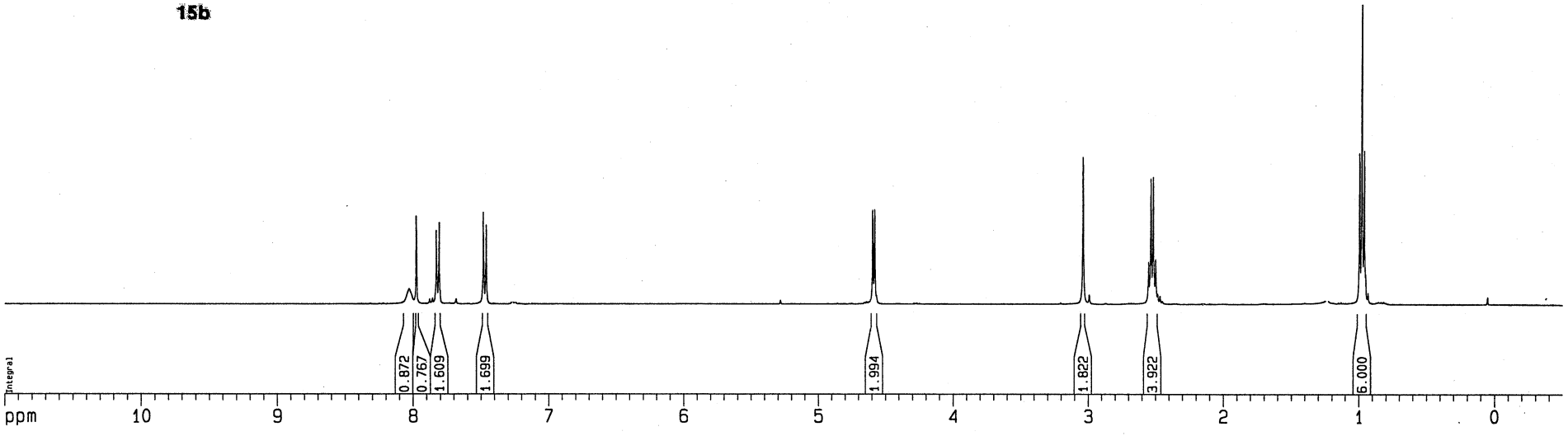
15a

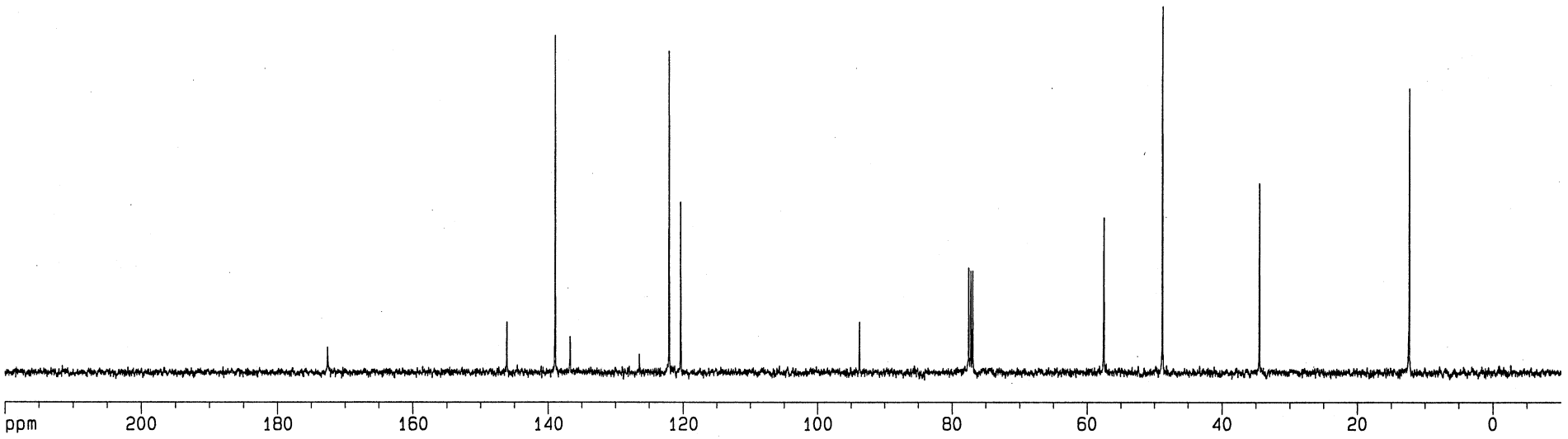
Integral
0.938
0.782
2.073
2.109
1.979
3.222
1.744
4.112
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

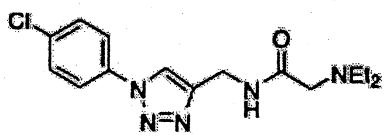

ppm
200
180
160
140
120
100
80
60
40
20
0


I
N
N=N
O
N
H
NEt2

15b

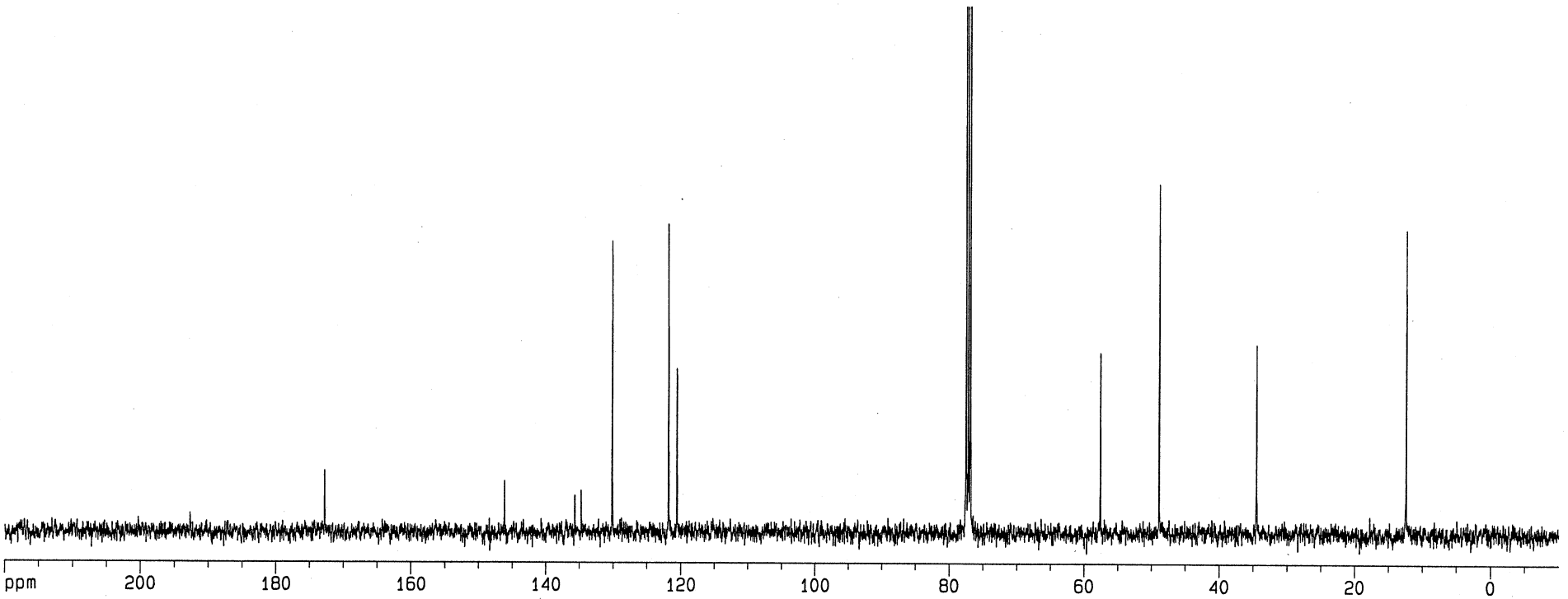

Integral
0.872
0.767
1.609
1.699
1.994
1.822
3.922
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

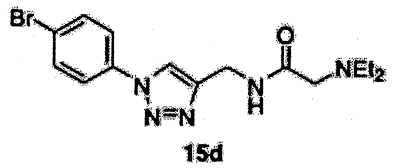

ppm
200
180
160
140
120
100
80
60
40
20
0


Cl
N
N=N
O
NH
NEt2

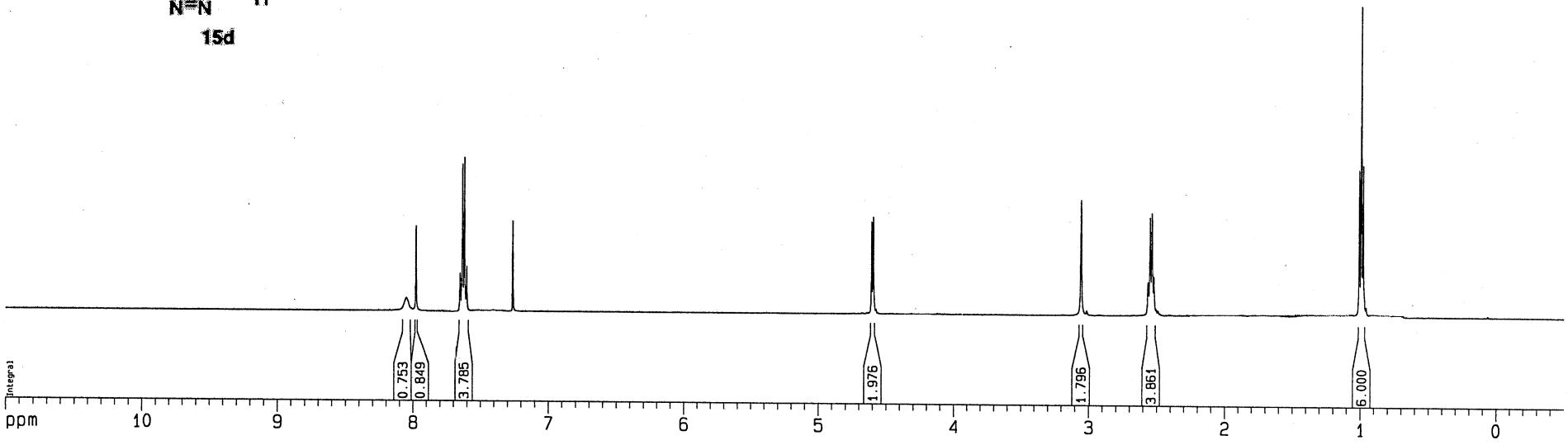
15c

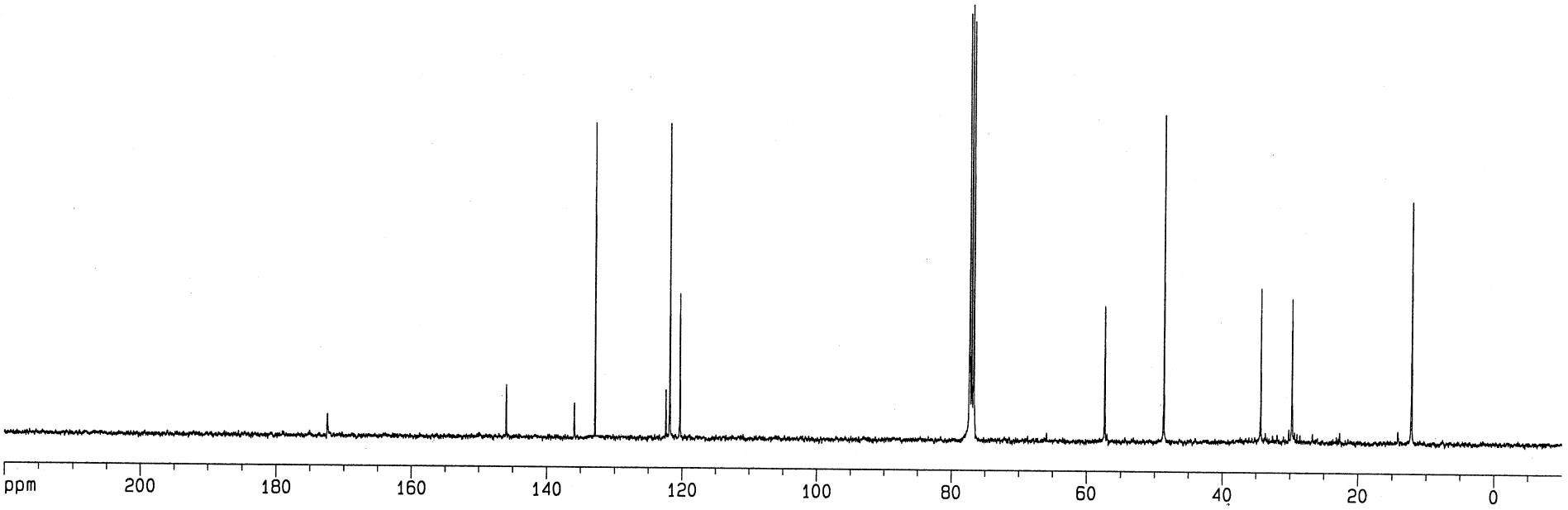
Integral
0.850
0.882
1.839
1.792
2.042
2.004
4.096
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

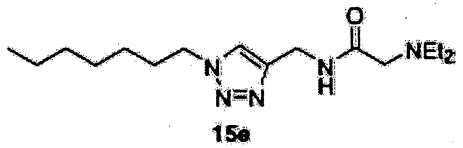

ppm
200
180
160
140
120
100
80
60
40
20
0


Br
N
N=N
N
H
O
NEt2

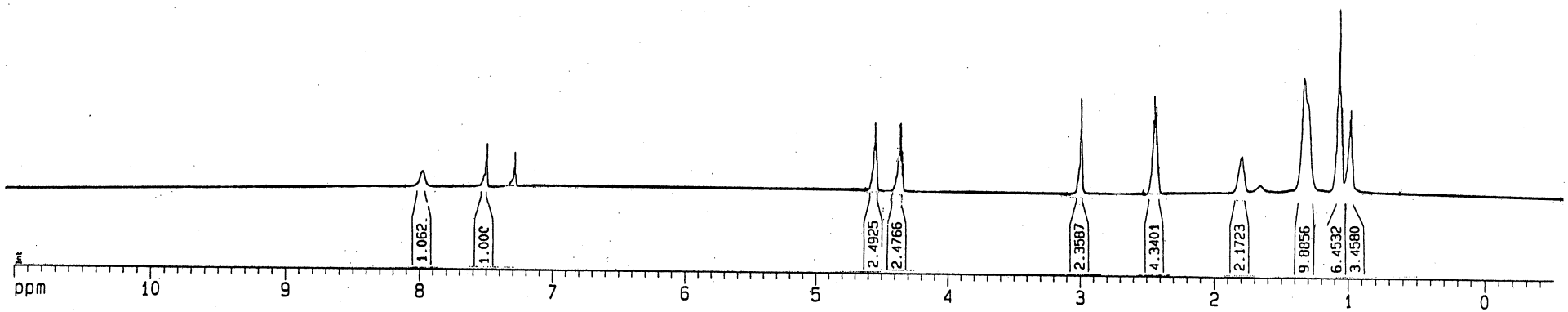
15d

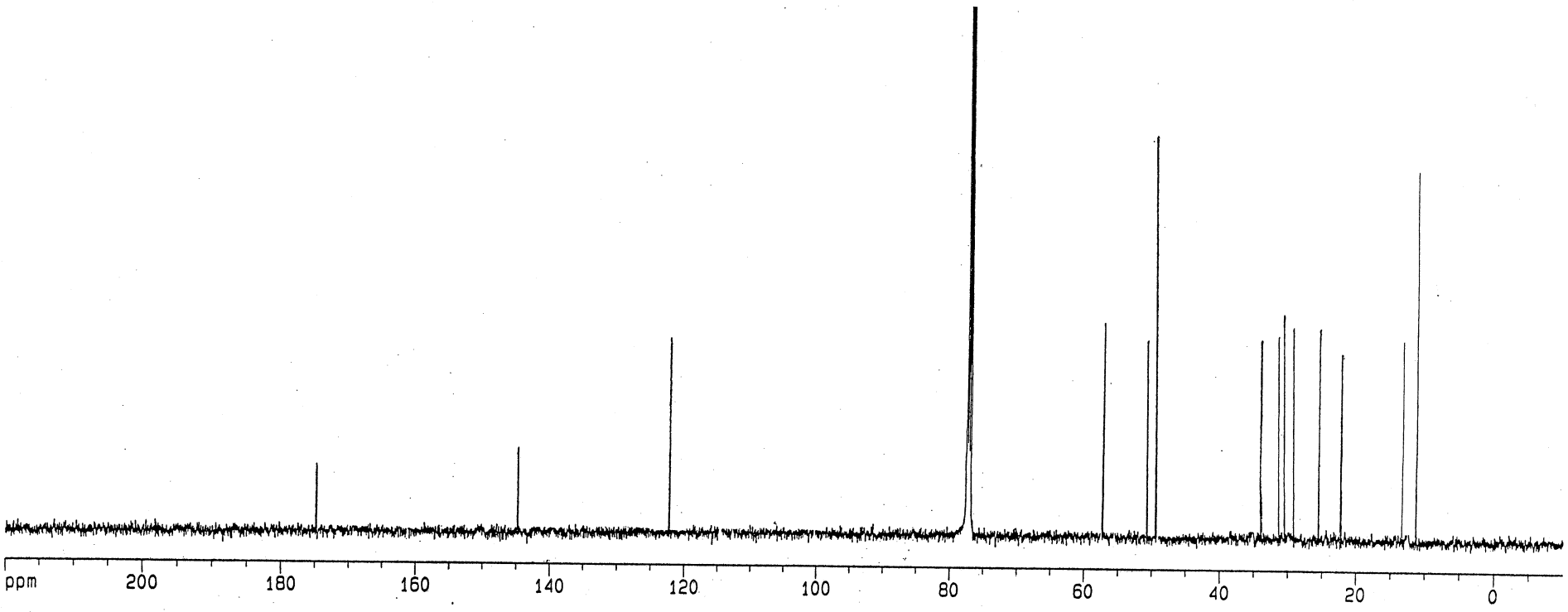

Integral
0.753
0.849
3.785
1.976
1.796
3.861
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

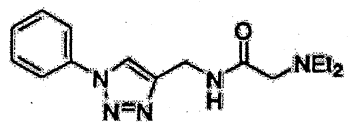

ppm
200
180
160
140
120
100
80
60
40
20
0


O
NEt2
N
N
N=N
H

15e

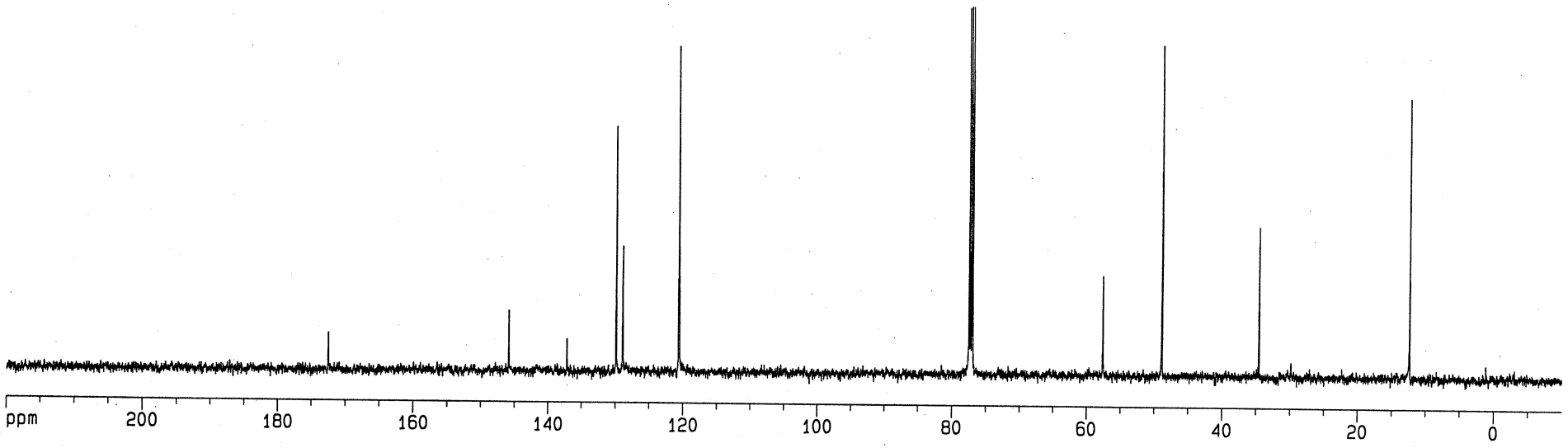

1.062
1.000
2.4925
2.4766
2.3587
4.3401
2.1723
9.8856
6.4532
3.4580
ppm
10
9
8
7
6
5
4
3
2
1
0

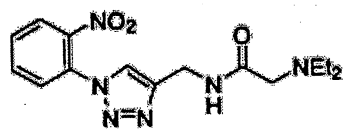

ppm
200
180
160
140
120
100
80
60
40
20
0


O
NEt2
N
N
N=N
H

15f

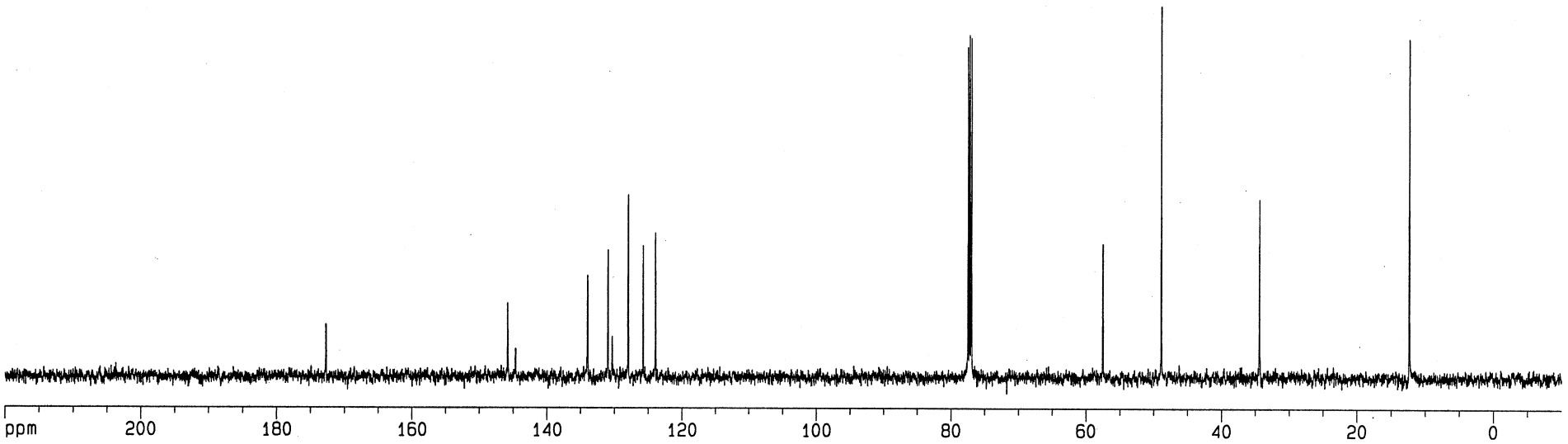
Integral
0.812
0.999
1.870
1.891
0.877
2.048
2.026
0.741
4.076
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

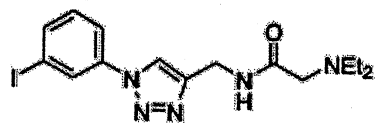

ppm
200
180
160
140
120
100
80
60
40
20
0


NO2
N
N=N
O
N
H
NEt2

15g

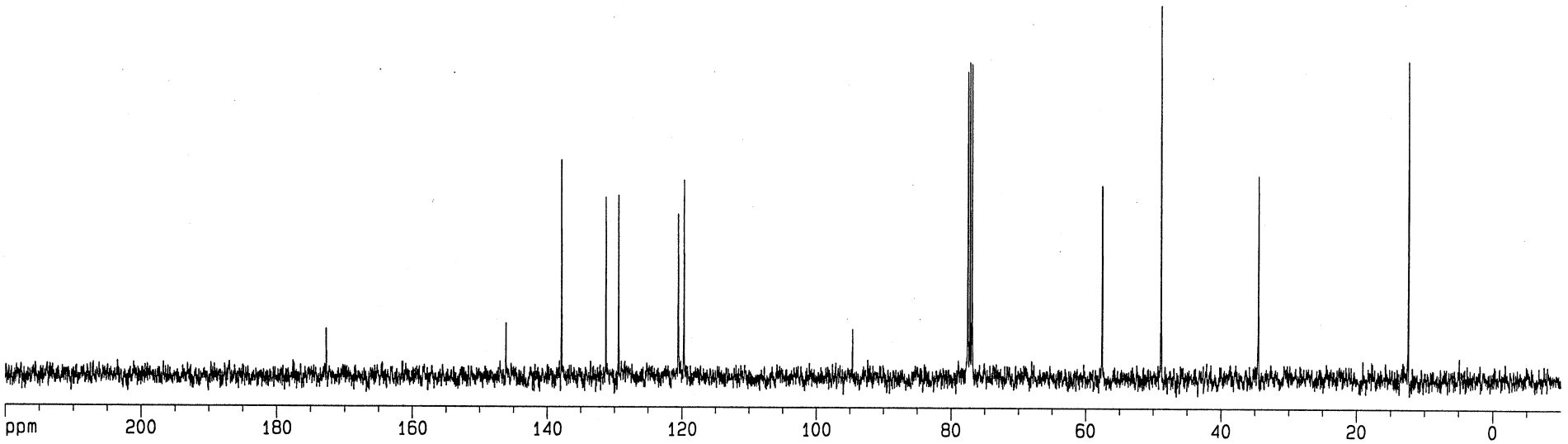
Integral
1.574
0.822
1.036
0.991
0.978
1.938
1.952
4.213
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

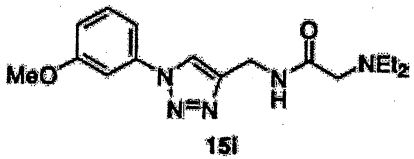

ppm
200
180
160
140
120
100
80
60
40
20
0


I
N
N=N
N
H
O
NEt2

15h

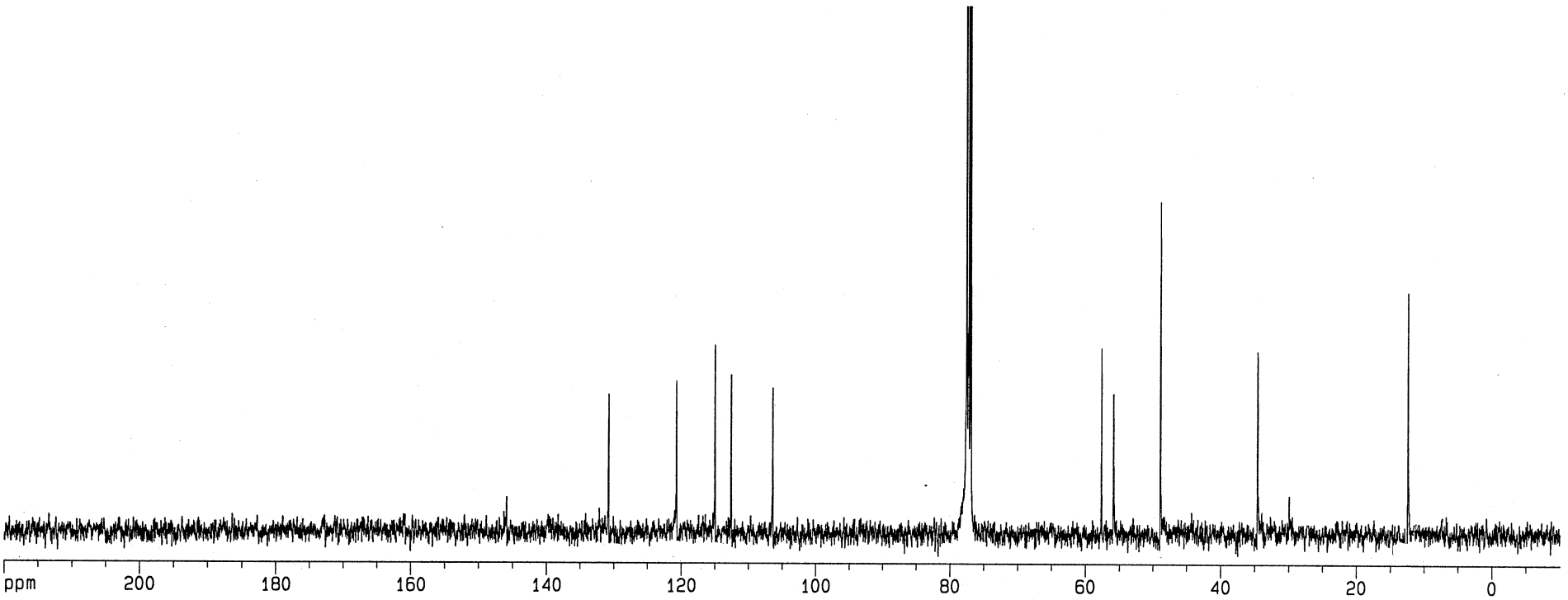
Integral
0.785
0.830
0.930
0.794
0.925
1.136
1.975
1.936
4.079
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

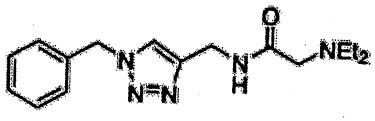

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
N
N=N
N
H
O
NEt2

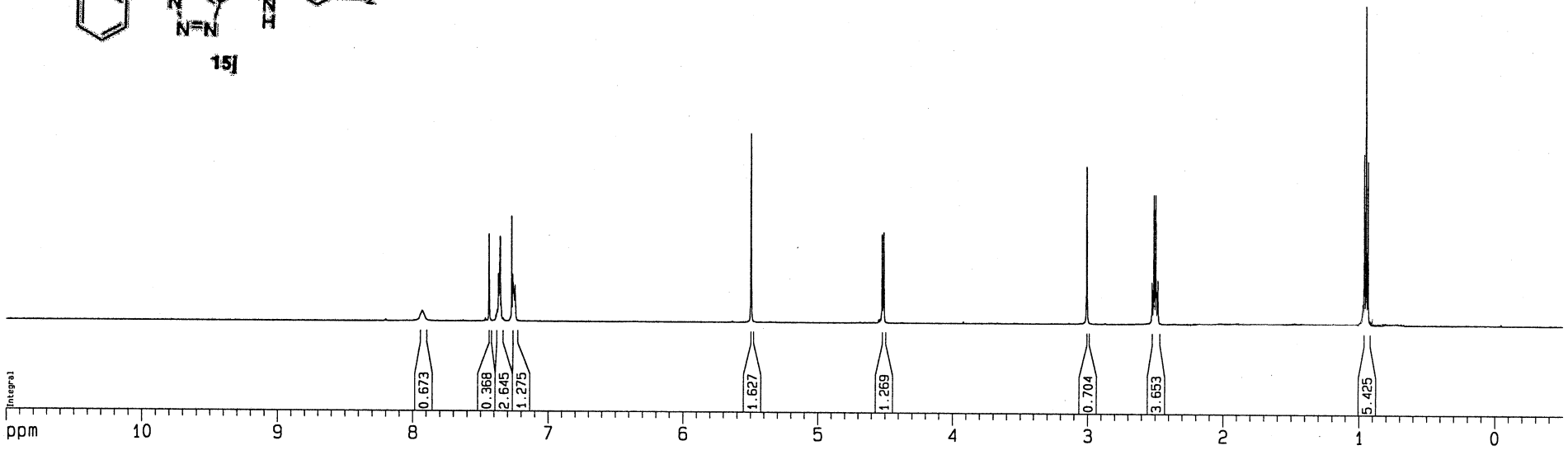
15l

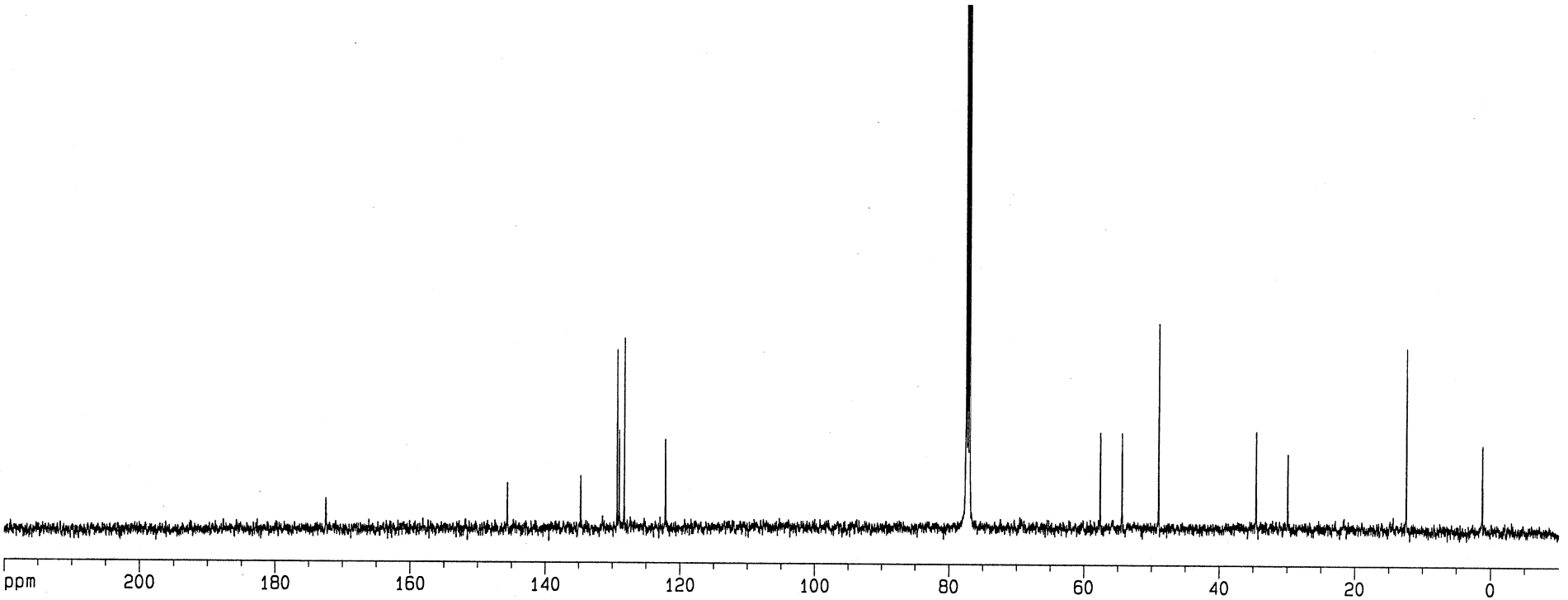
Integral
0.854
0.762
0.930
0.796
0.798
1.890
2.624
1.808
3.966
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

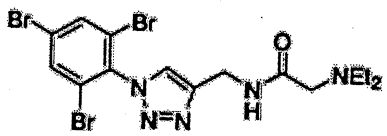

ppm
200
180
160
140
120
100
80
60
40
20
0


O
NEt2
N
N=N
H

15j

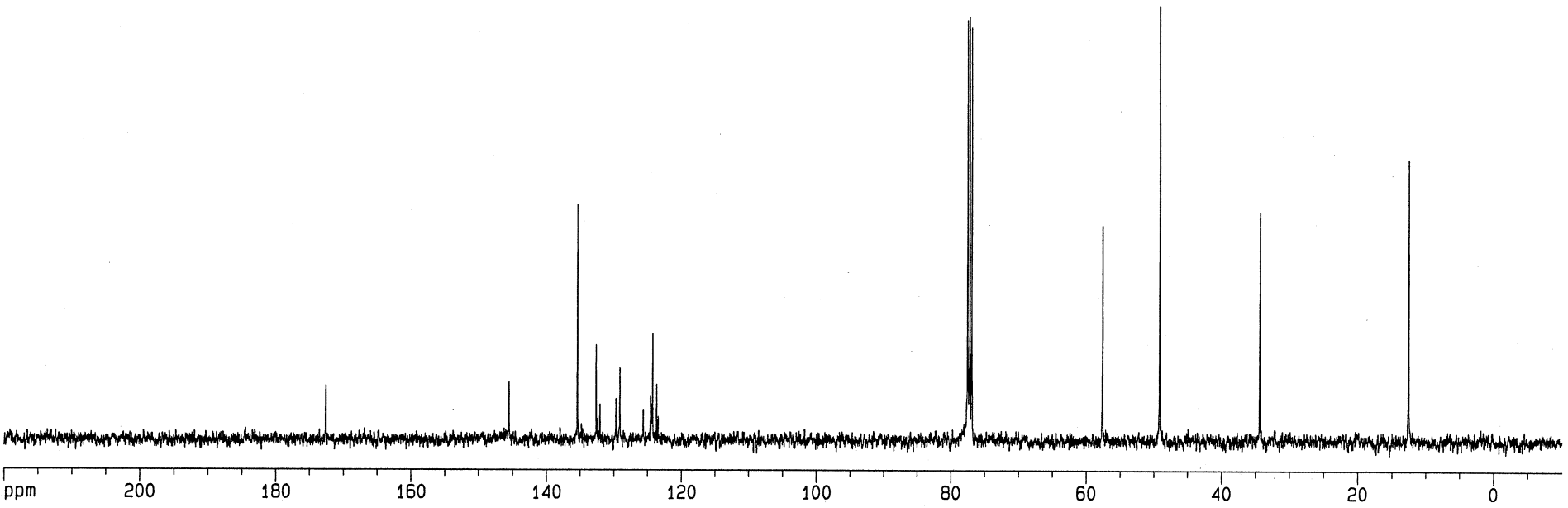

Integral
0.673
0.368
2.645
1.275
1.627
1.269
0.704
3.653
5.425
ppm
10
9
8
7
6
5
4
3
2
1
0

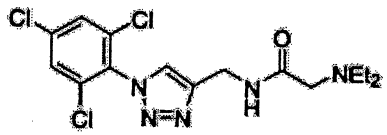

ppm
200
180
160
140
120
100
80
60
40
20
0


Br
Br
Br
N
N=N
O
N
H
NEt2

15k

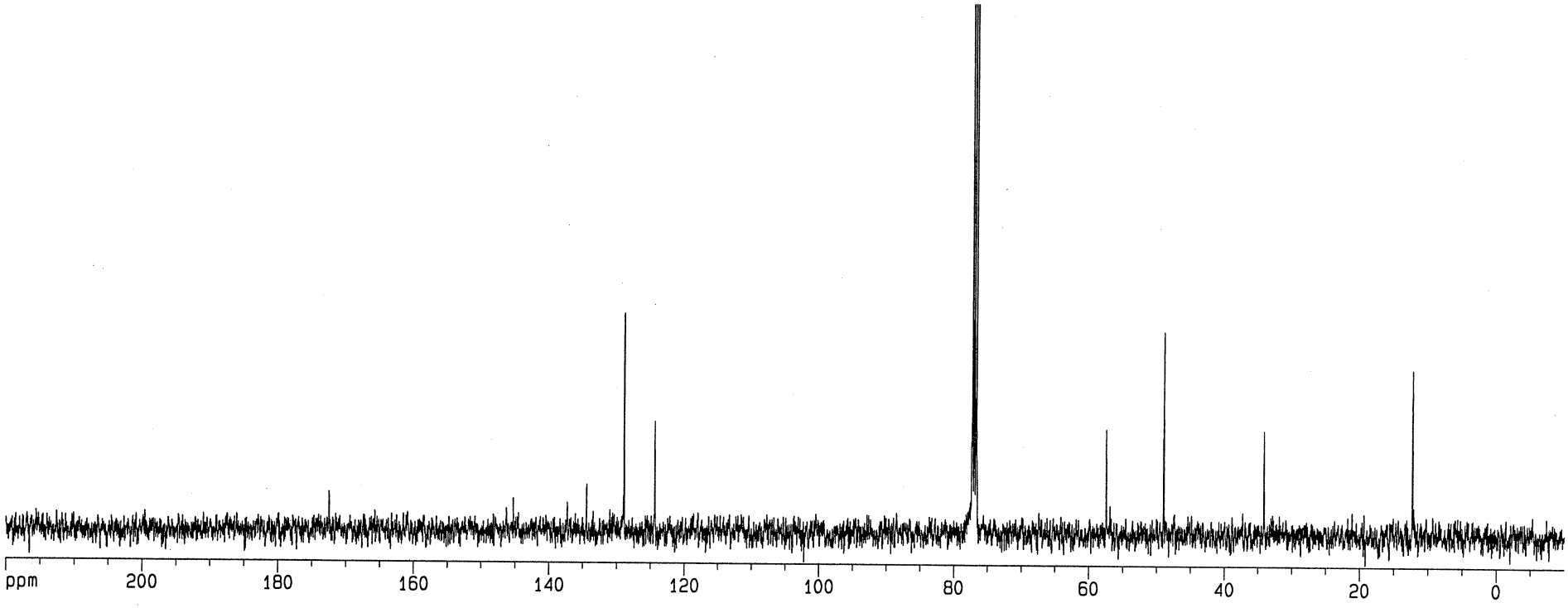
Integral
0.865
0.626
0.584
2.021
2.005
4.075
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

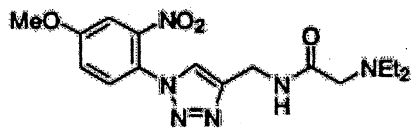

ppm
200
180
160
140
120
100
80
60
40
20
0


Cl
Cl
Cl
N
N=N
N
H
O
NEt2

151

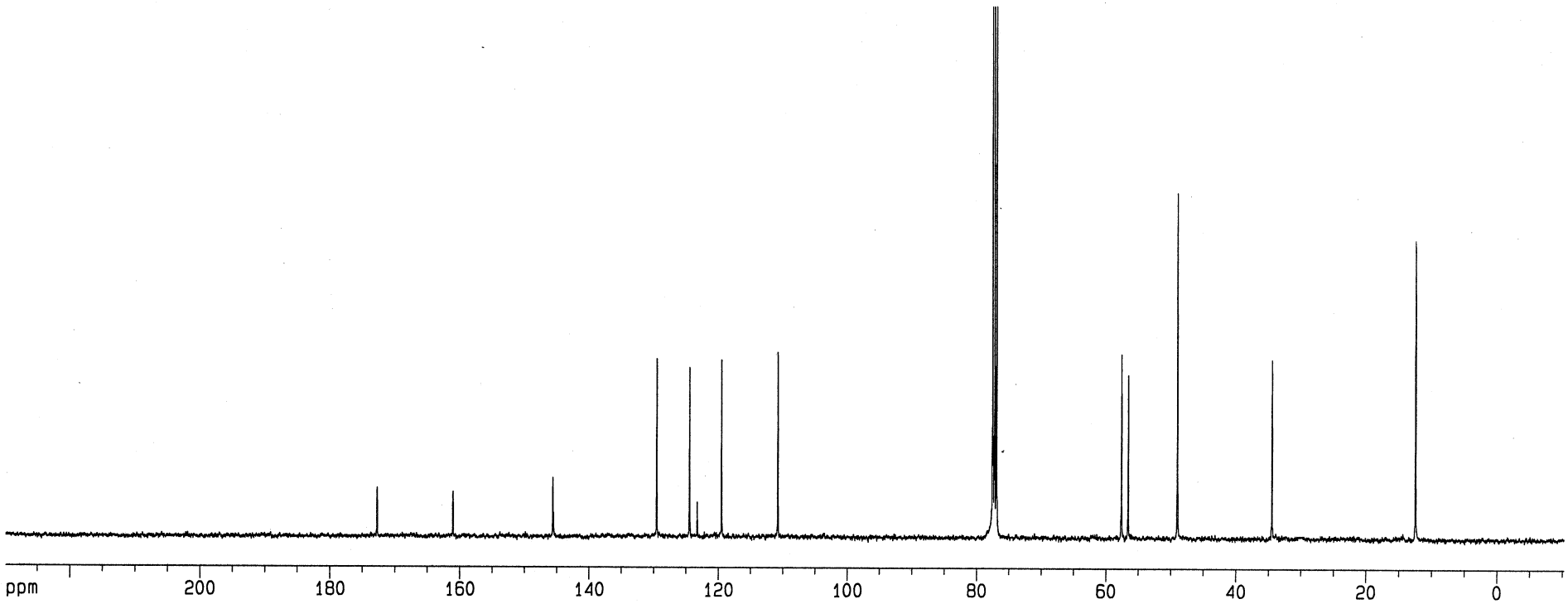
Integral
0.817
0.676
1.131
1.954
1.925
4.116
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

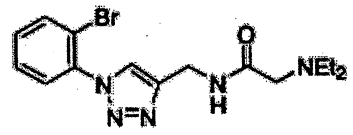

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
NO2
O
NEt2
N
N
N=N
H

15m

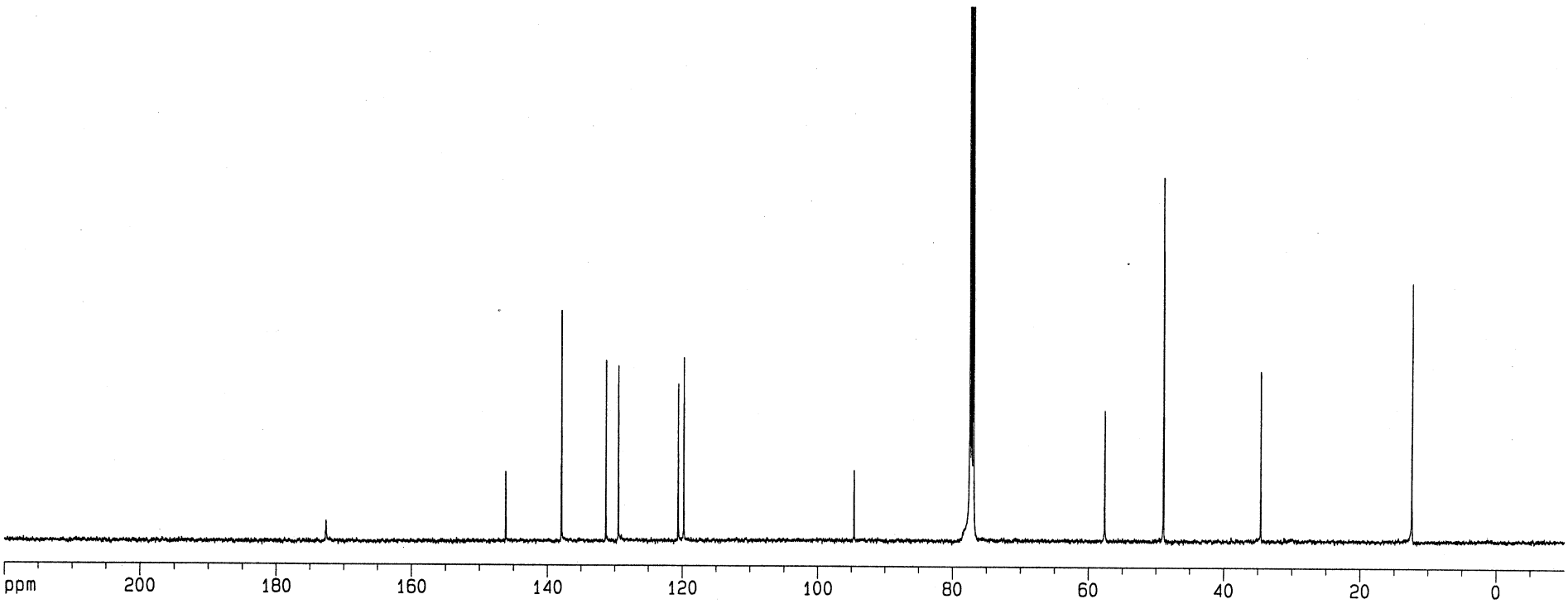
Integral
0.885
0.755
0.764
0.845
1.201
1.923
2.741
1.928
4.085
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

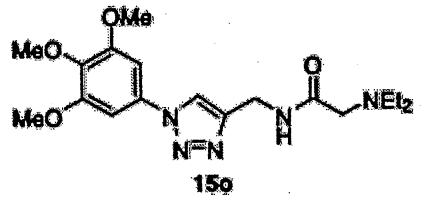

ppm
200
180
160
140
120
100
80
60
40
20
0


Br
N
N=N
O
N
H
NEt2

15n

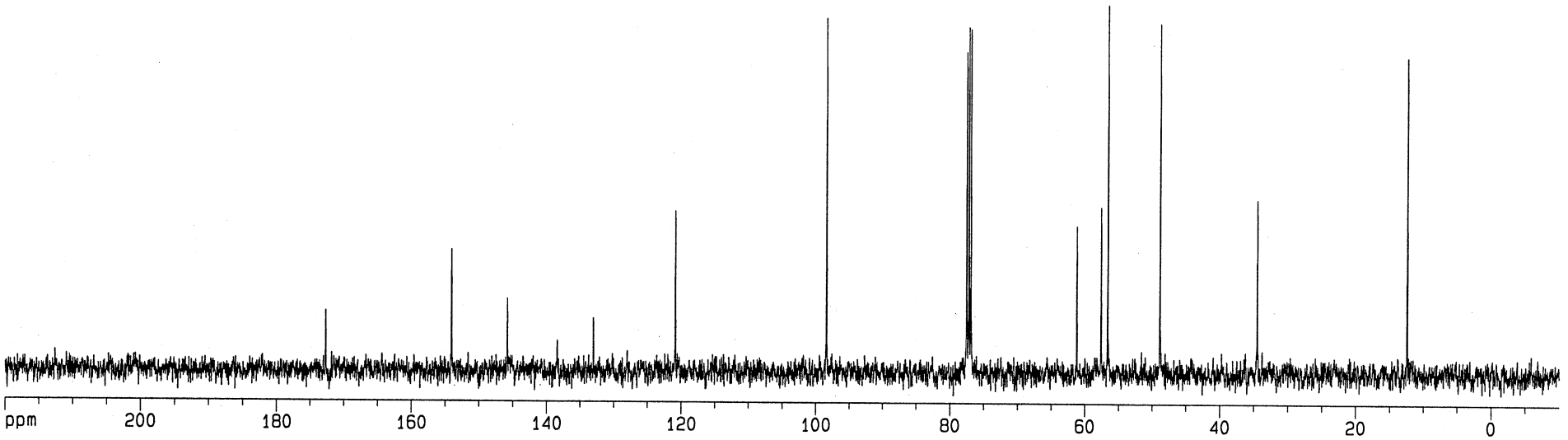
Integral
0.875
0.884
0.954
0.893
0.984
0.726
2.008
1.819
4.010
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

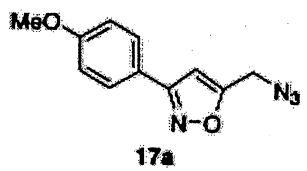

ppm
200
180
160
140
120
100
80
60
40
20
0


OMe
MeO
MeO
O
NEt2
N
N
N
H

15o

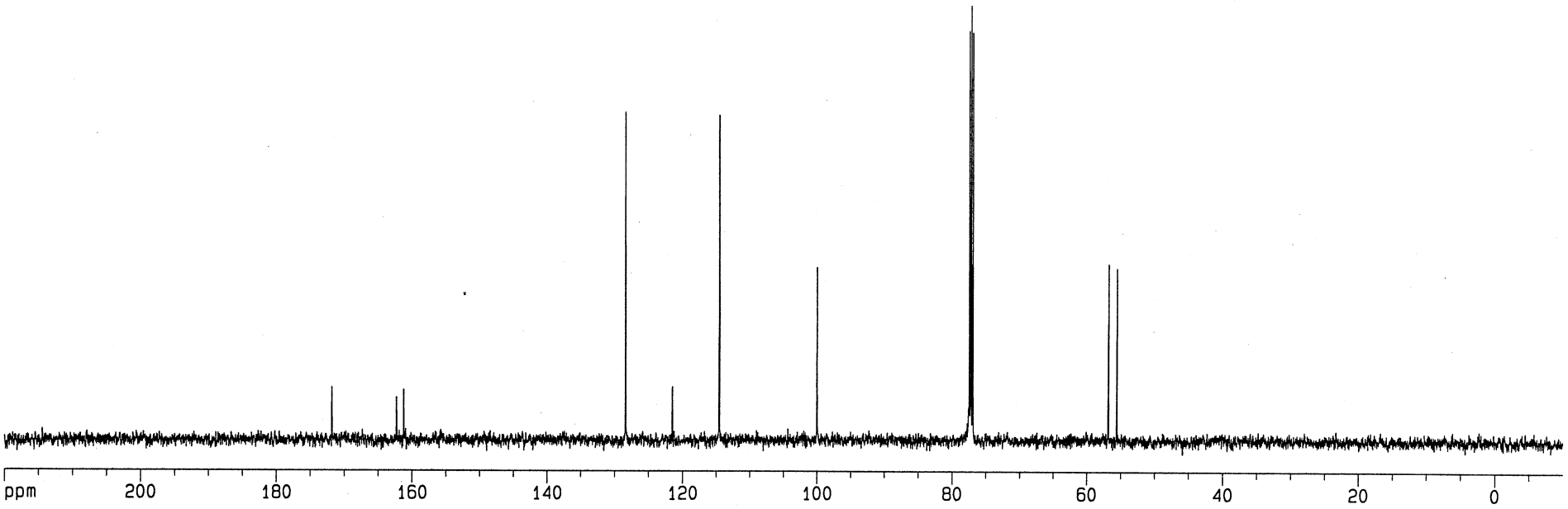
Integral
0.945
0.882
2.057
2.008
6.922
3.470
1.948
4.217
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

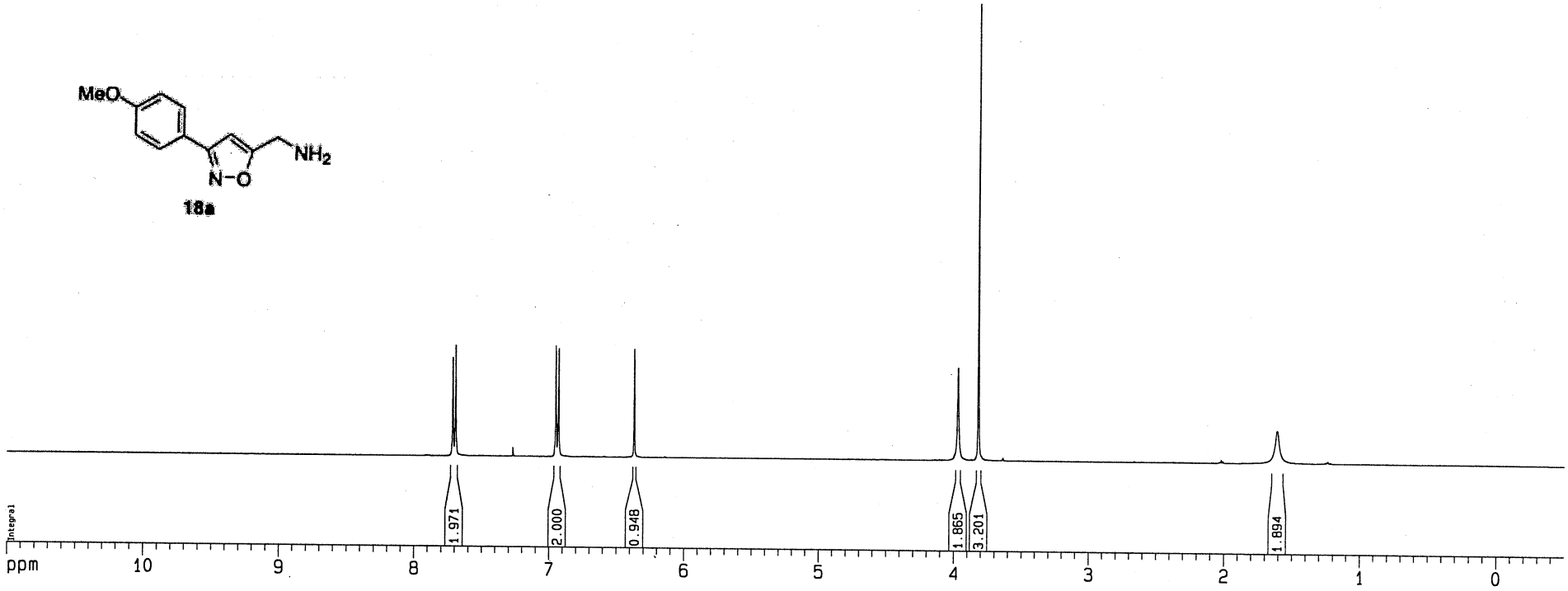

ppm
200
180
160
140
120
100
80
60
40
20
0

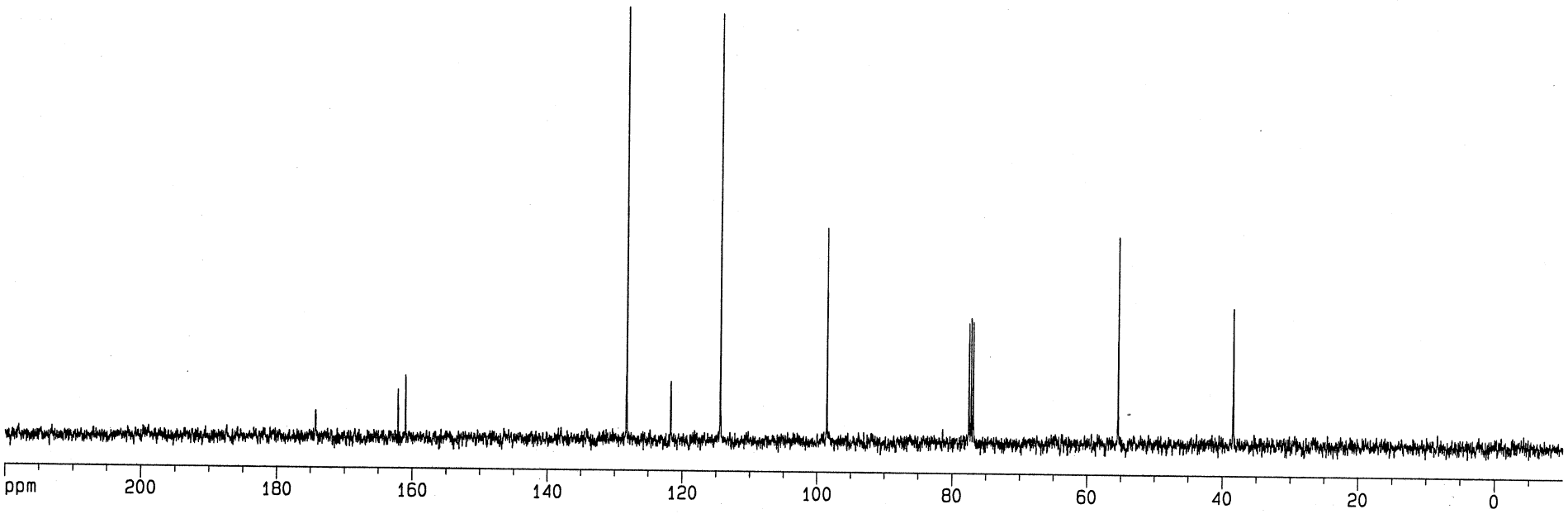

MeO
N
O
N_3

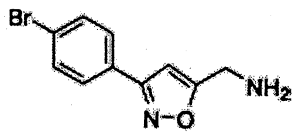
17a

Integral
1.882
2.000
0.952
2.070
3.399
ppm
10
9
8
7
6
5
4
3
2
1
0

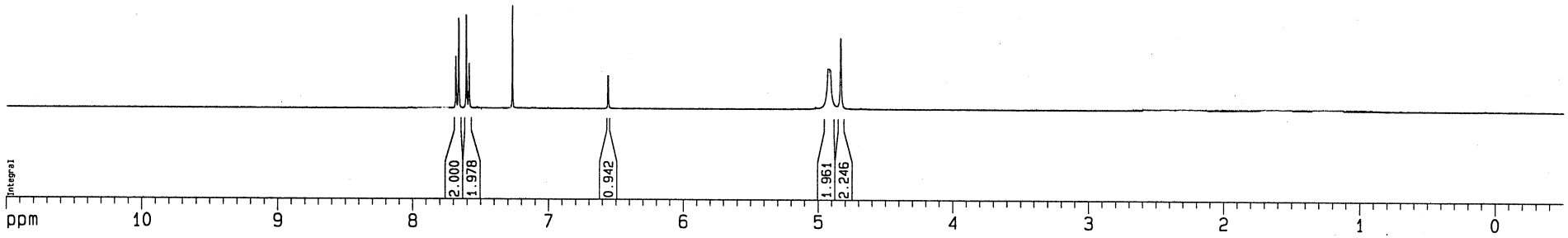

ppm
200
180
160
140
120
100
80
60
40
20
0

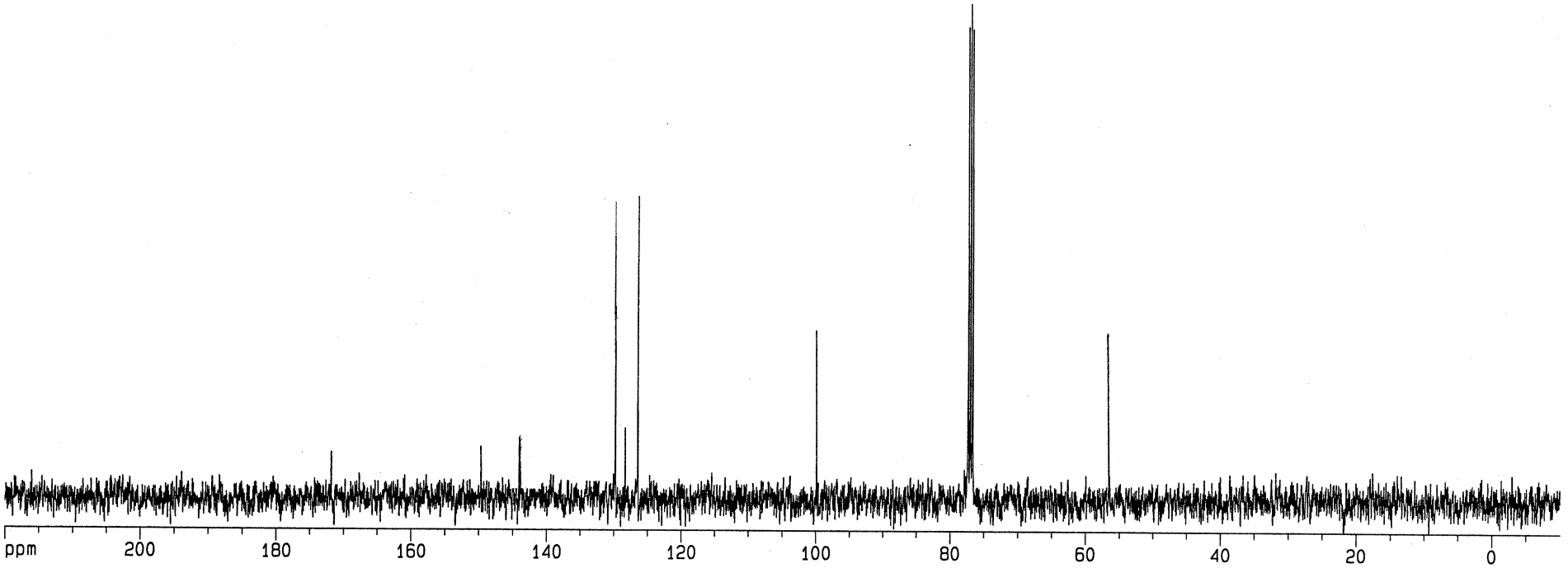

MeO
NH2
N–O
18a
Integral
1.971
2.000
0.948
1.865
3.201
1.894
ppm
10
9
8
7
6
5
4
3
2
1
0

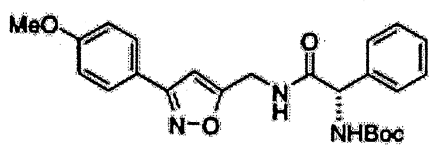

ppm
200
180
160
140
120
100
80
60
40
20
0


Br
NH2
N
O

18b

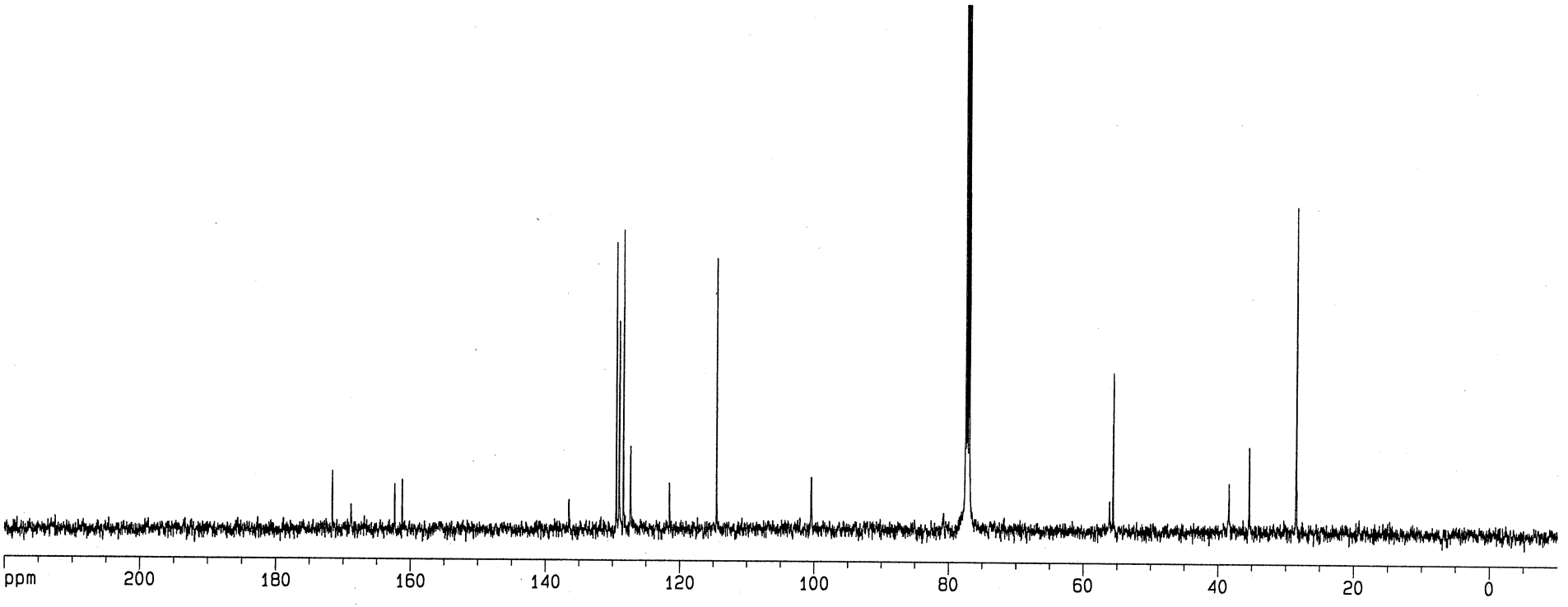

Integral
2.000
1.978
0.942
1.961
2.246
ppm
10
9
8
7
6
5
4
3
2
1
0

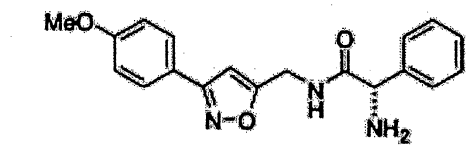

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
O
N
H
N–O
NHBoc

20a

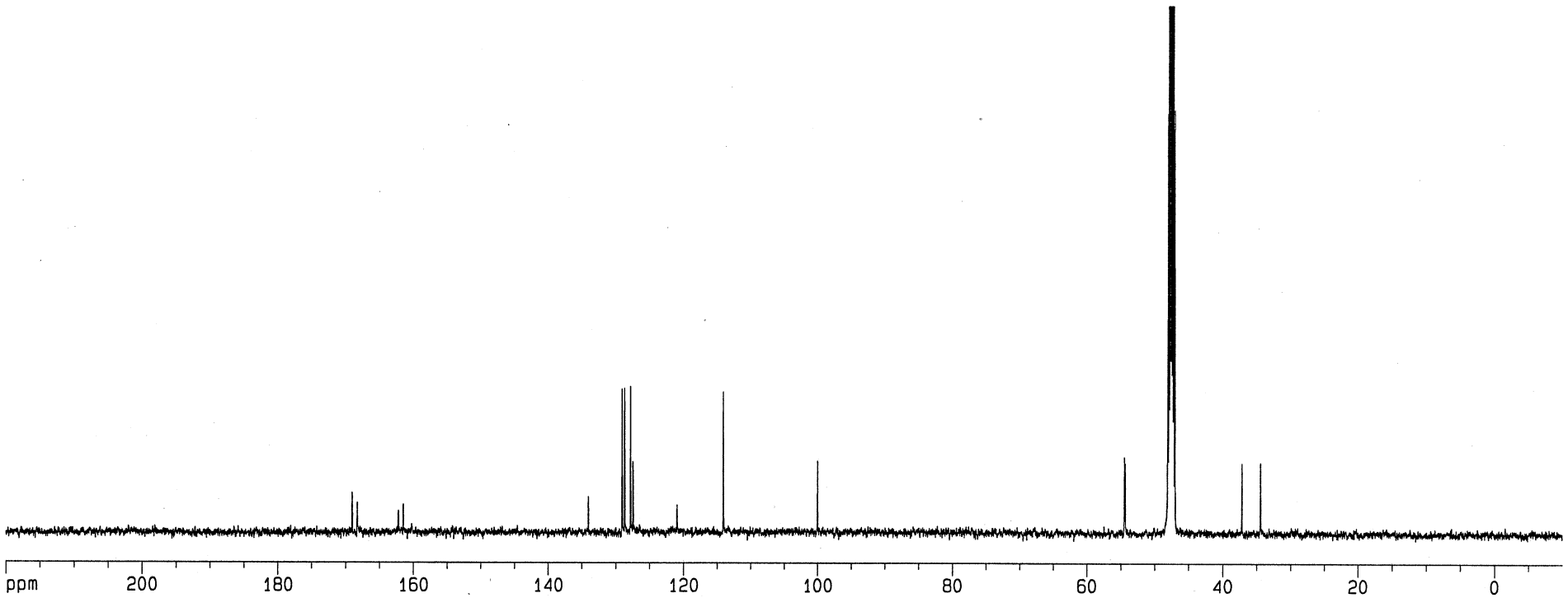
Integral
1.869
3.023
1.162
1.973
1.904
0.952
0.797
1.955
3.000
1.708
8.232
ppm
10
9
8
7
6
5
4
3
2
1
0

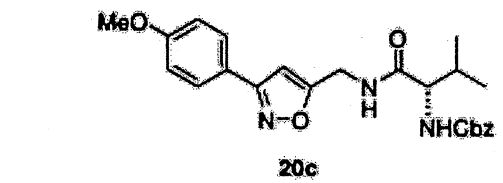

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
O
N
H
N–O
NH2

20b

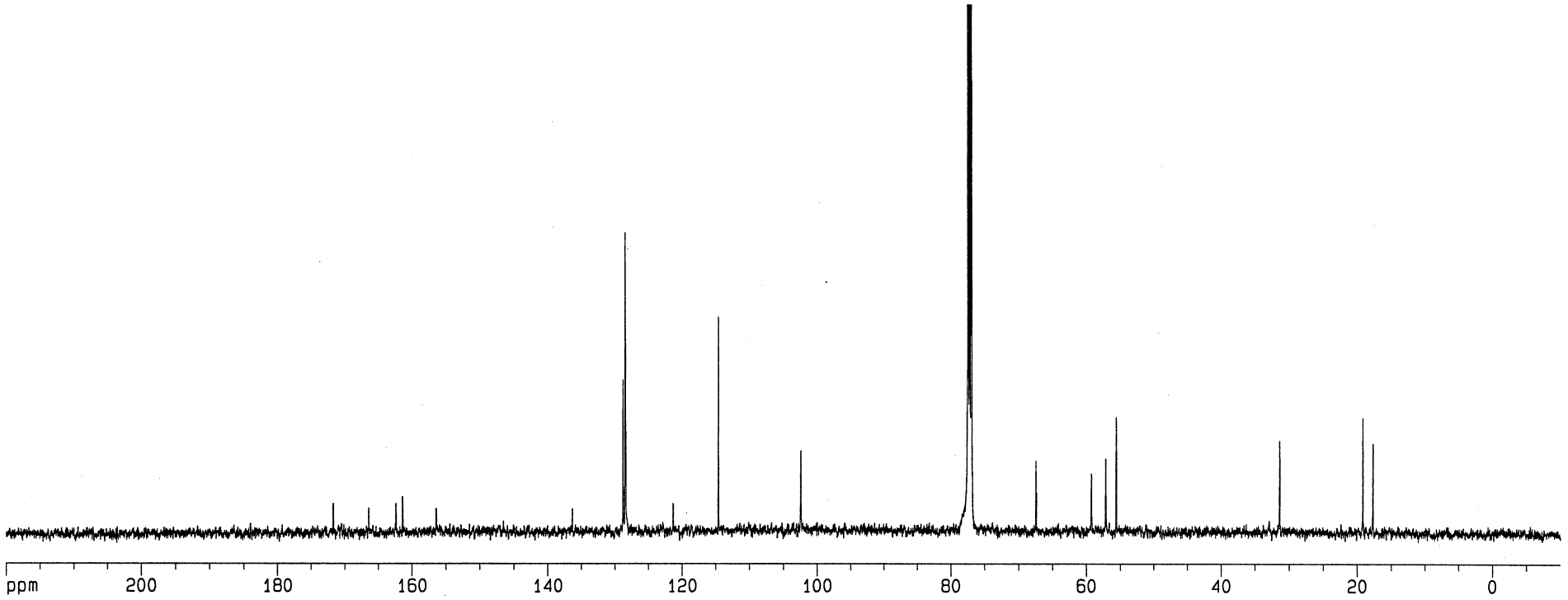
Integral
1.905
2.702
2.775
1.817
0.947
1.072
1.022
1.060
3.000
1.141
1.134
ppm
10
9
8
7
6
5
4
3
2
1
0

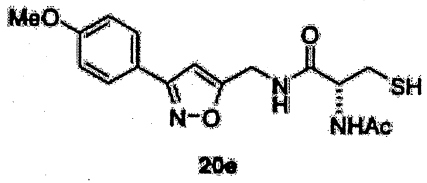

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
O
N
H
N–O
NHCbz

20c

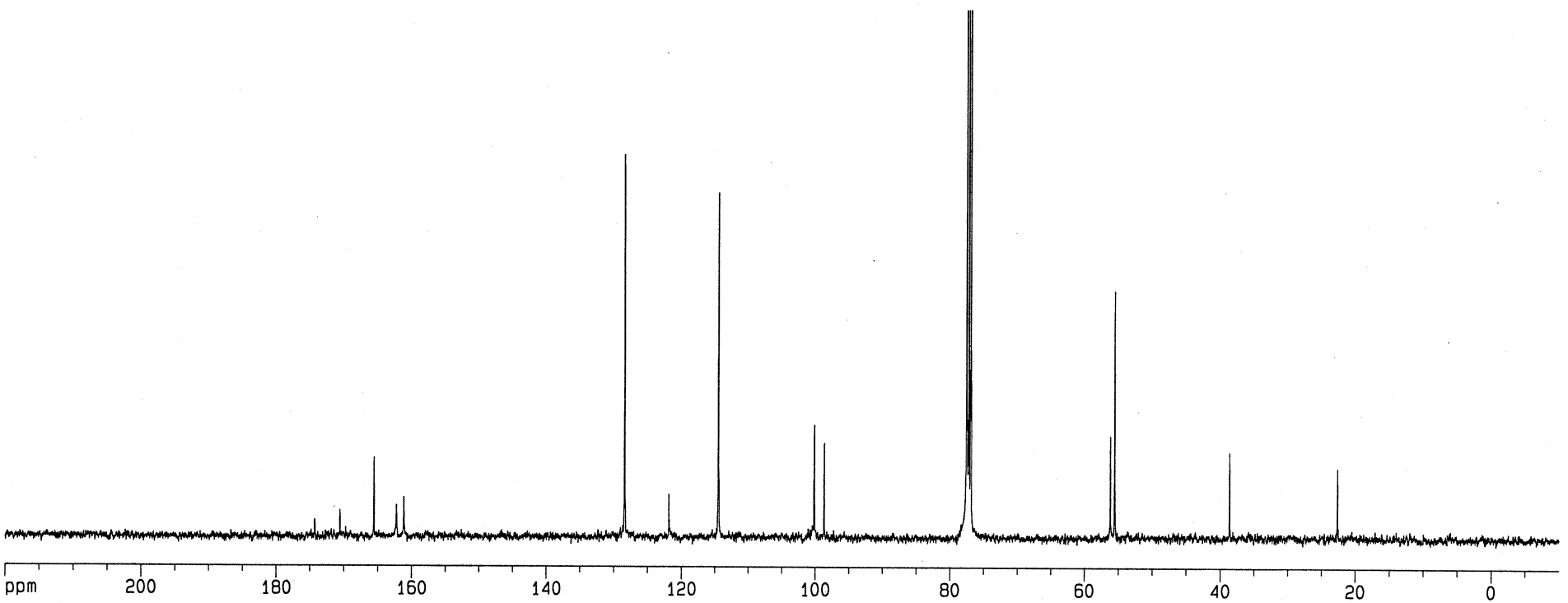
Integral
1.697
5.082
1.856
0.711
0.904
1.070
1.773
2.817
0.956
1.011
2.880
3.000
ppm
10
9
8
7
6
5
4
3
2
1
0

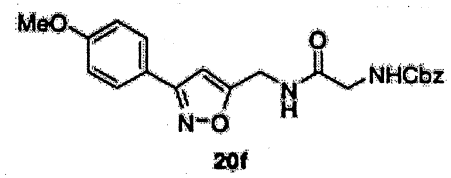

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
O
N
H
SH
N–O
NHAc

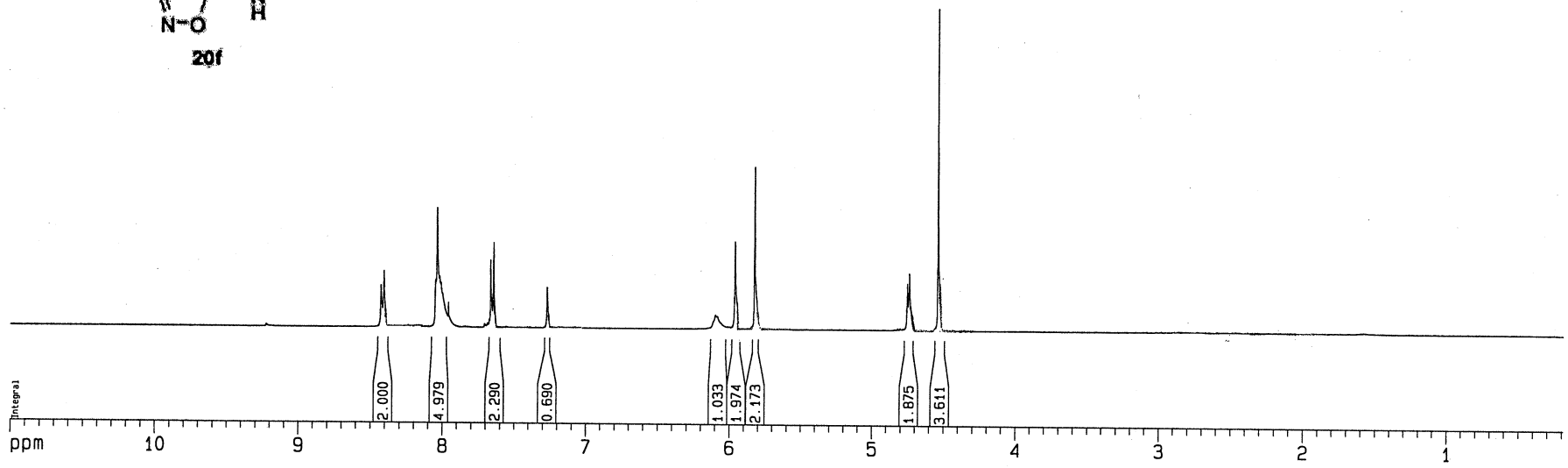
20e

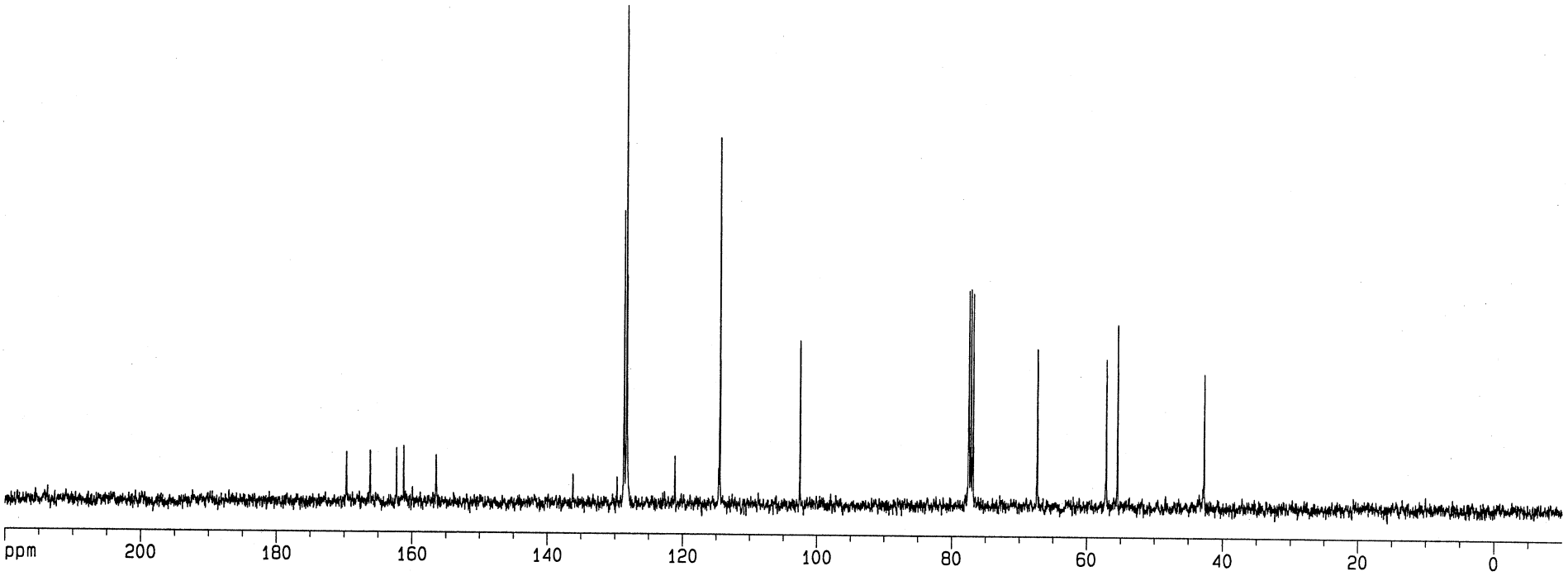
Integral
2.000
2.074
0.439
0.475
0.943
0.880
3.423
1.152
1.158
ppm
10
9
8
7
6
5
4
3
2
1
0

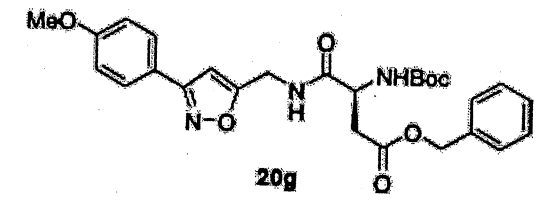

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
O
NHCbz
N
H
N-O

20f

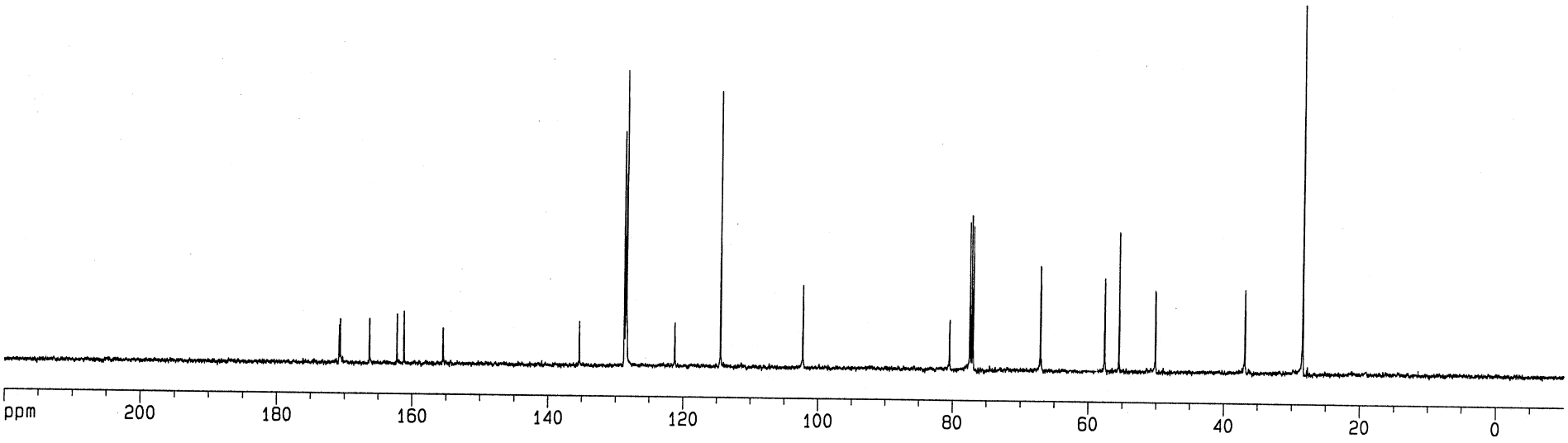

Integral
2.000
4.979
2.290
0.690
1.033
1.974
2.173
1.875
3.611
ppm
10
9
8
7
6
5
4
3
2
1

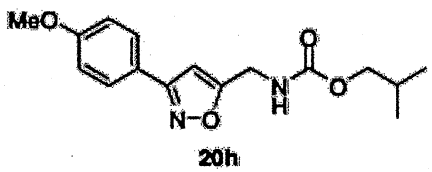

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
N-O
N
H
O
NHBoc
O
O

20g

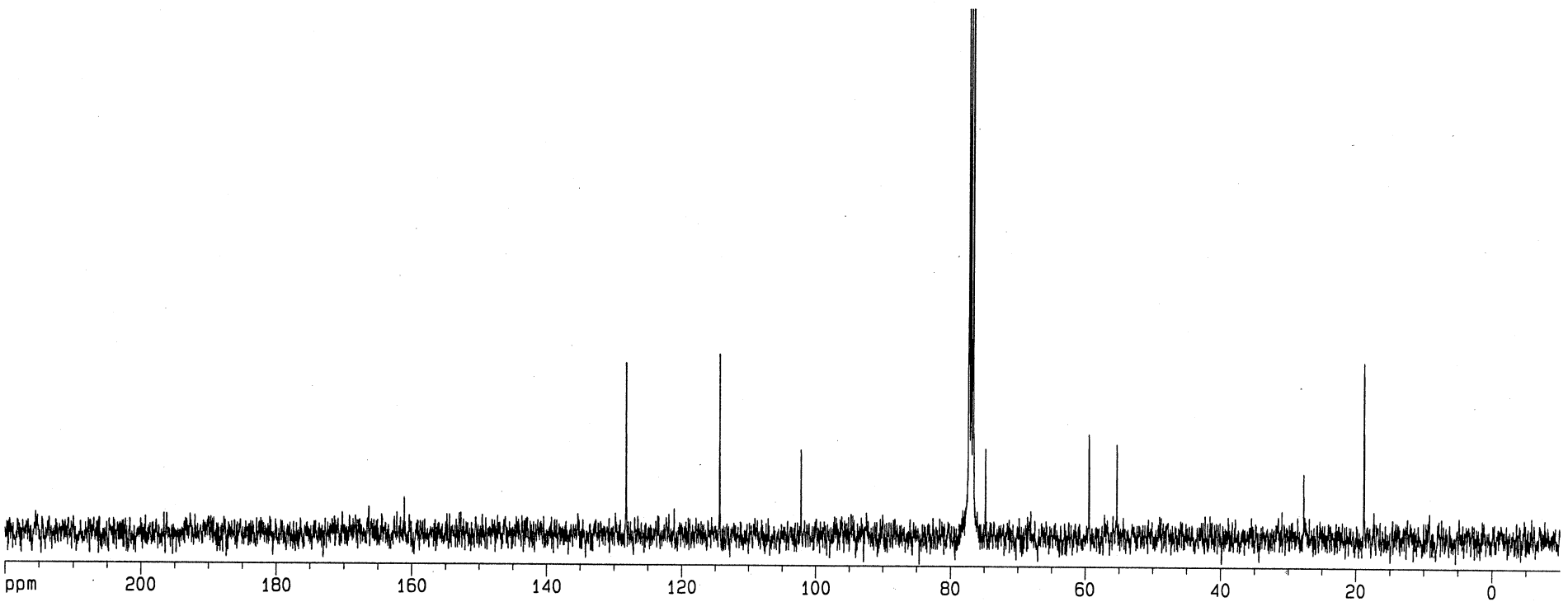
Integral
1.765
5.251
1.818
0.897
0.786
1.762
1.945
0.827
2.845
0.917
1.036
9.000
ppm
10
9
8
7
6
5
4
3
2
1
0

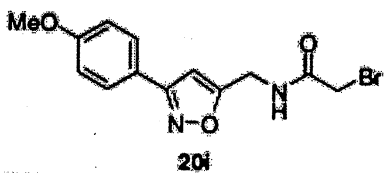

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
O
N
H
N–O
O

20h

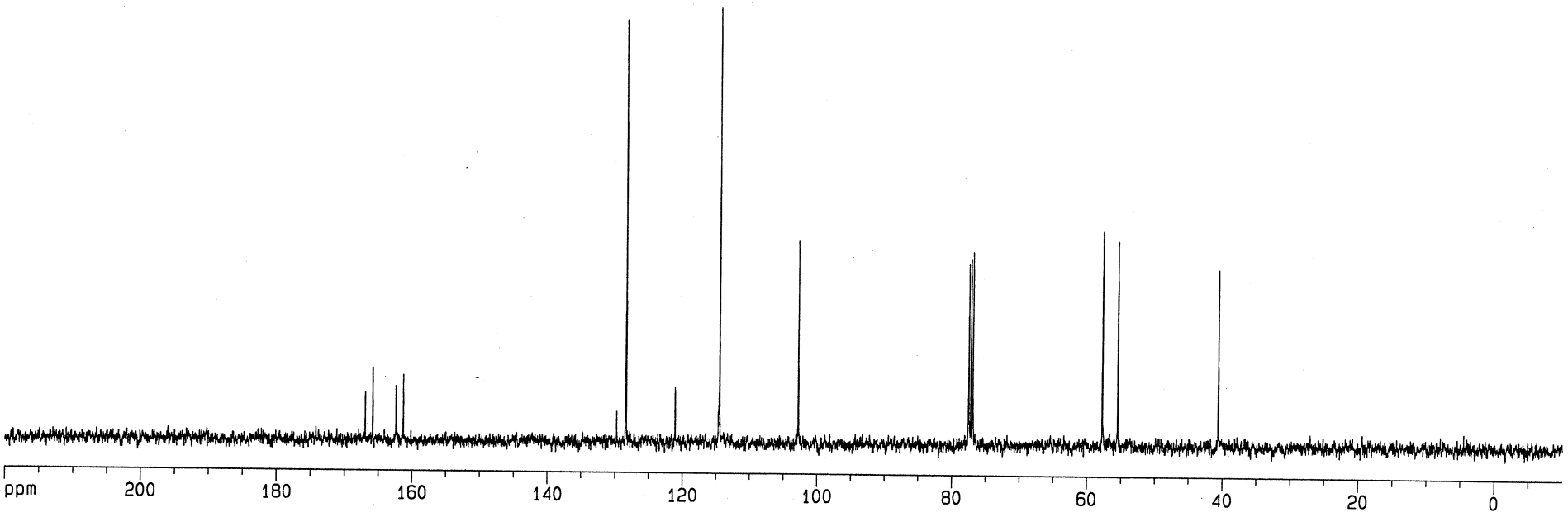
Integral
2.000
2.036
0.883
1.987
1.965
3.100
2.048
1.201
5.919
5.990
ppm
10
9
8
7
6
5
4
3
2
1
0

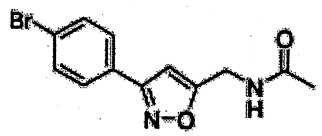

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
O
N
H
Br
N–O

20i

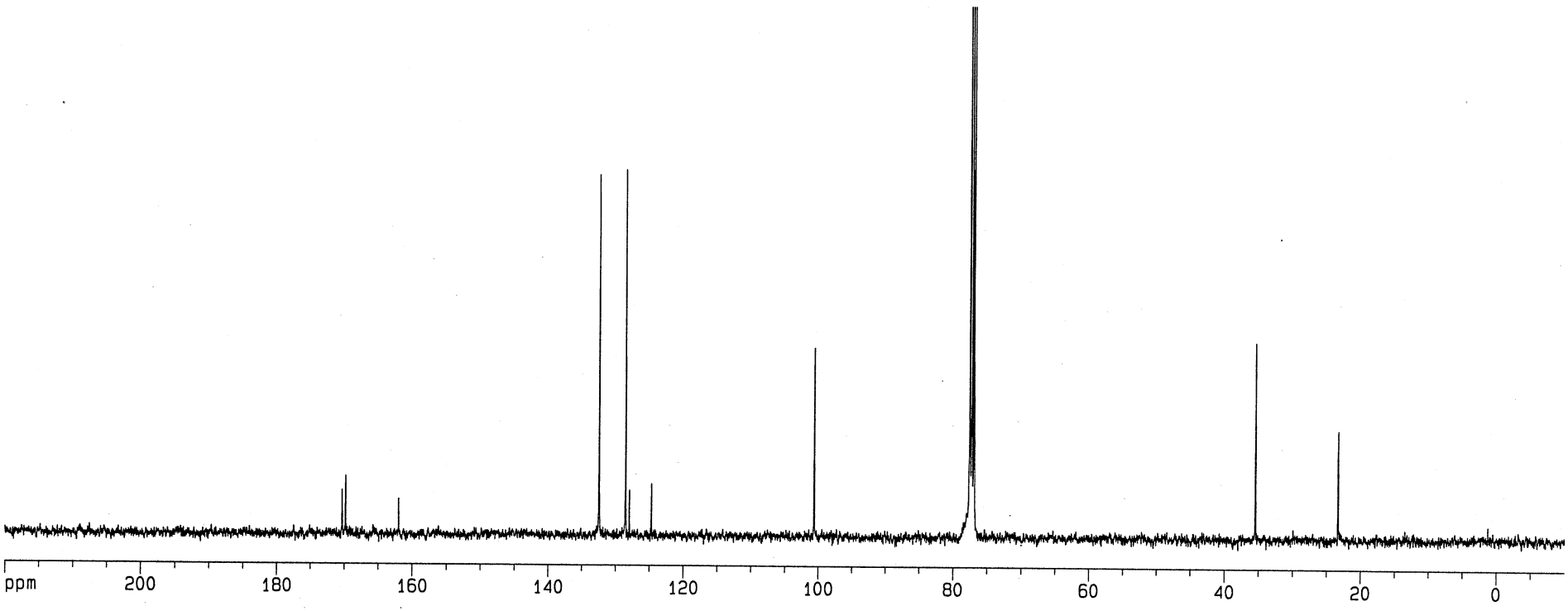
Integral
2.000
1.991
0.932
2.141
1.796
3.220
ppm
10
9
8
7
6
5
4
3
2
1
0

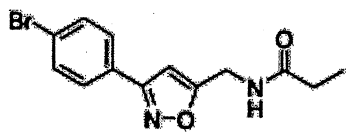

ppm
200
180
160
140
120
100
80
60
40
20
0


Br
O
N
H
N
O

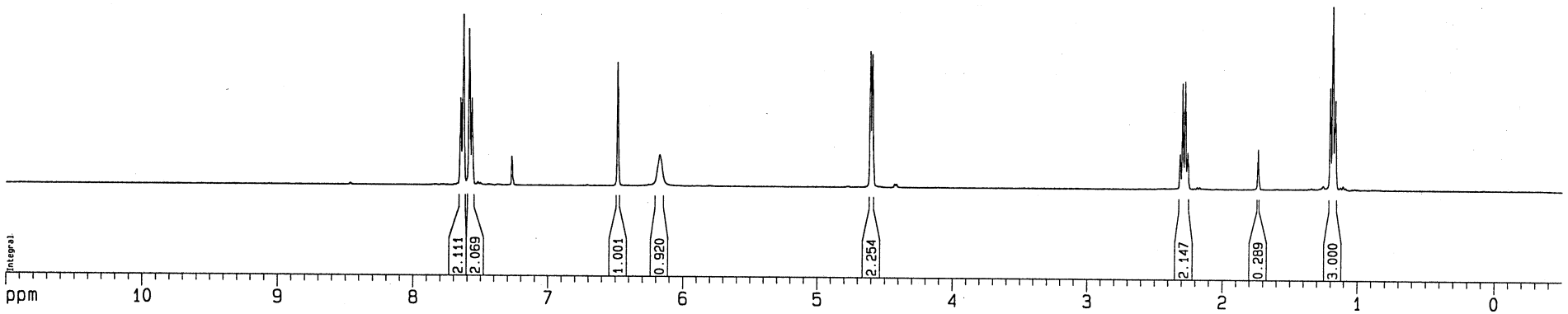
20j

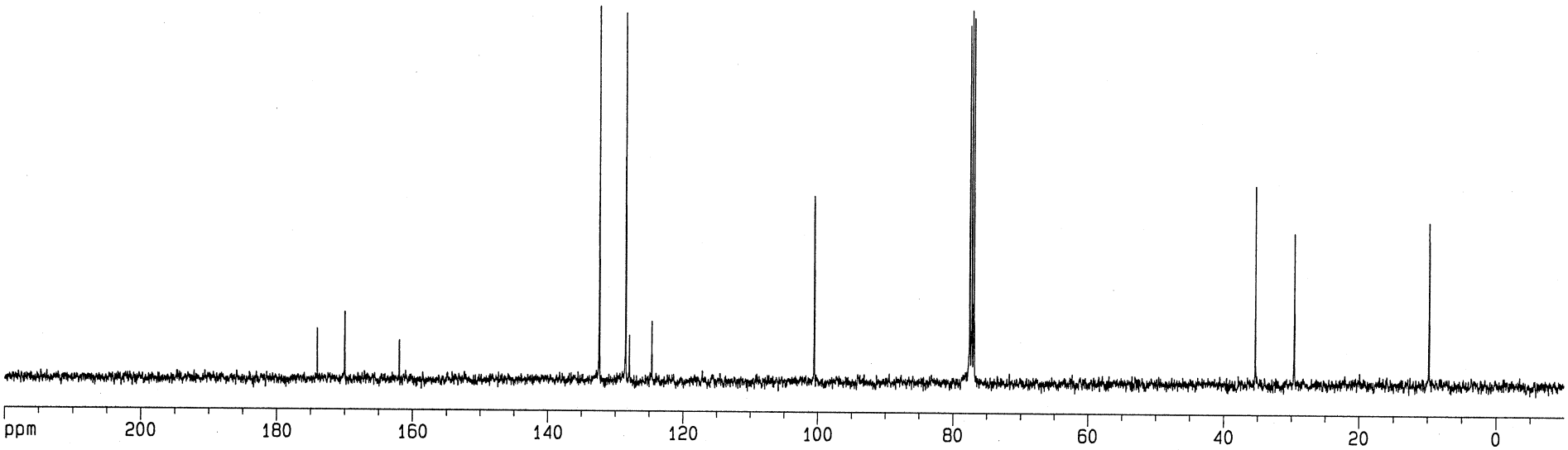
Integral
1.981
1.894
0.905
0.929
2.192
3.000
ppm
10
9
8
7
6
5
4
3
2
1
0

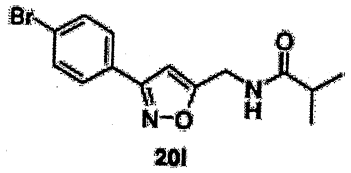

ppm
200
180
160
140
120
100
80
60
40
20
0


Br
O
N
H
N–O

20k

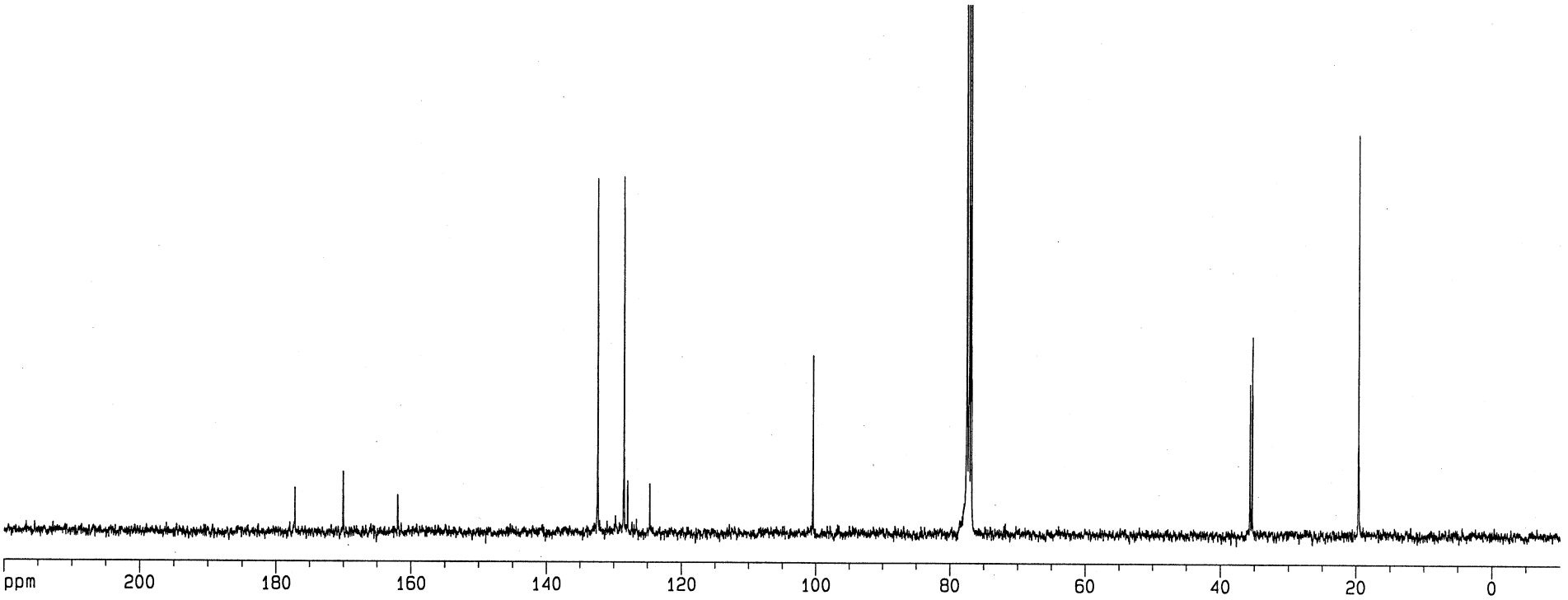

Integral
2.111
2.069
1.001
0.920
2.254
2.147
0.289
3.000
ppm
10
9
8
7
6
5
4
3
2
1
0

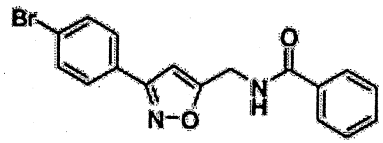

ppm
200
180
160
140
120
100
80
60
40
20
0


Br
O
N
H
N–O

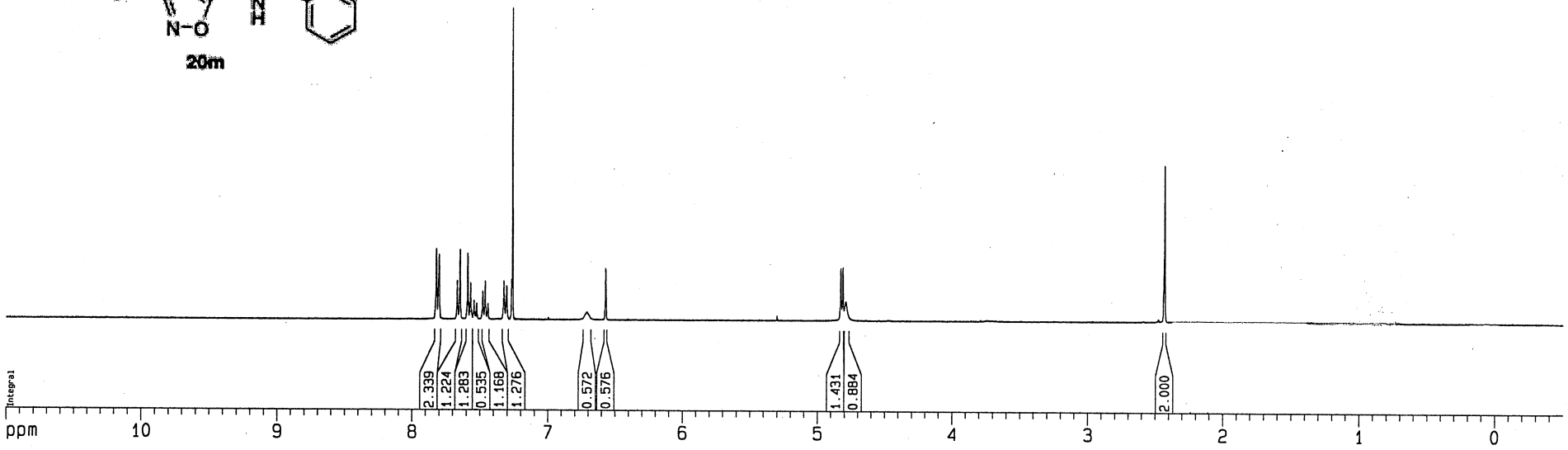
20l

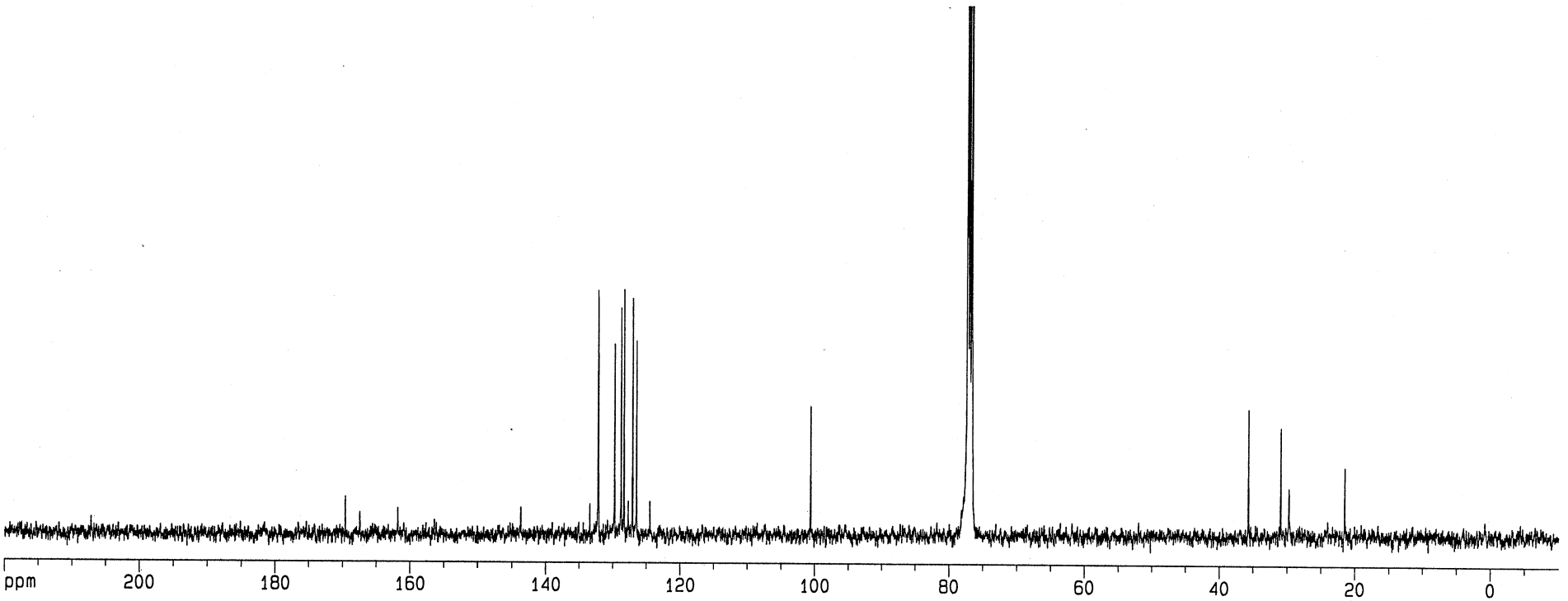
Integral
1.854
1.834
0.836
0.817
2.049
0.993
2.894
3.000
ppm
10
9
8
7
6
5
4
3
2
1
0

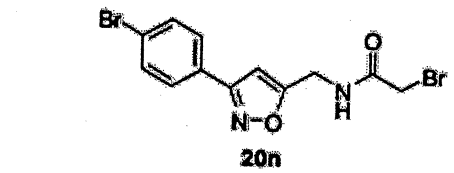

ppm
200
180
160
140
120
100
80
60
40
20
0


Br
O
N
H
N–O

20m

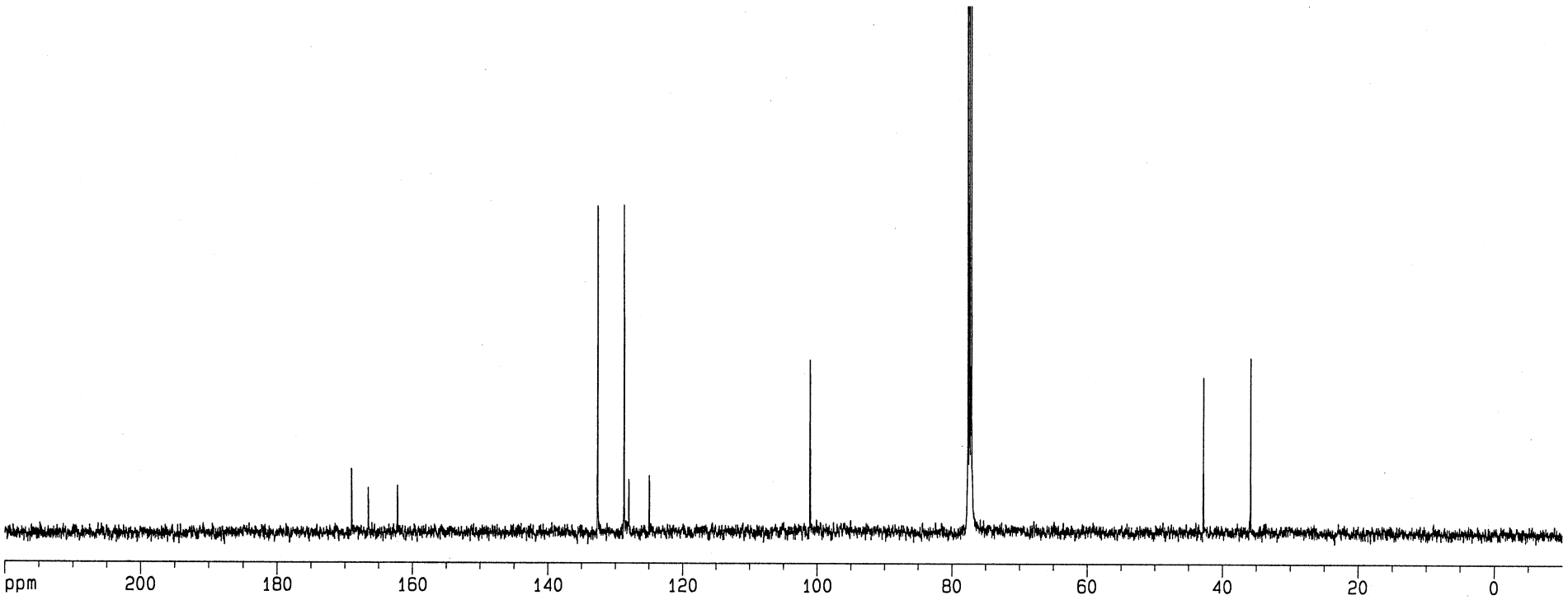

Integral
2.339
1.224
1.283
0.535
1.168
1.276
0.572
0.576
1.431
0.884
2.000
ppm
10
9
8
7
6
5
4
3
2
1
0

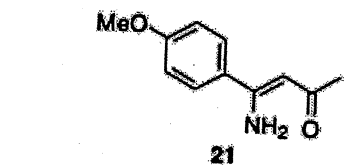

ppm
200
180
160
140
120
100
80
60
40
20
0


Br
O
Br
N
H
N–O

20n

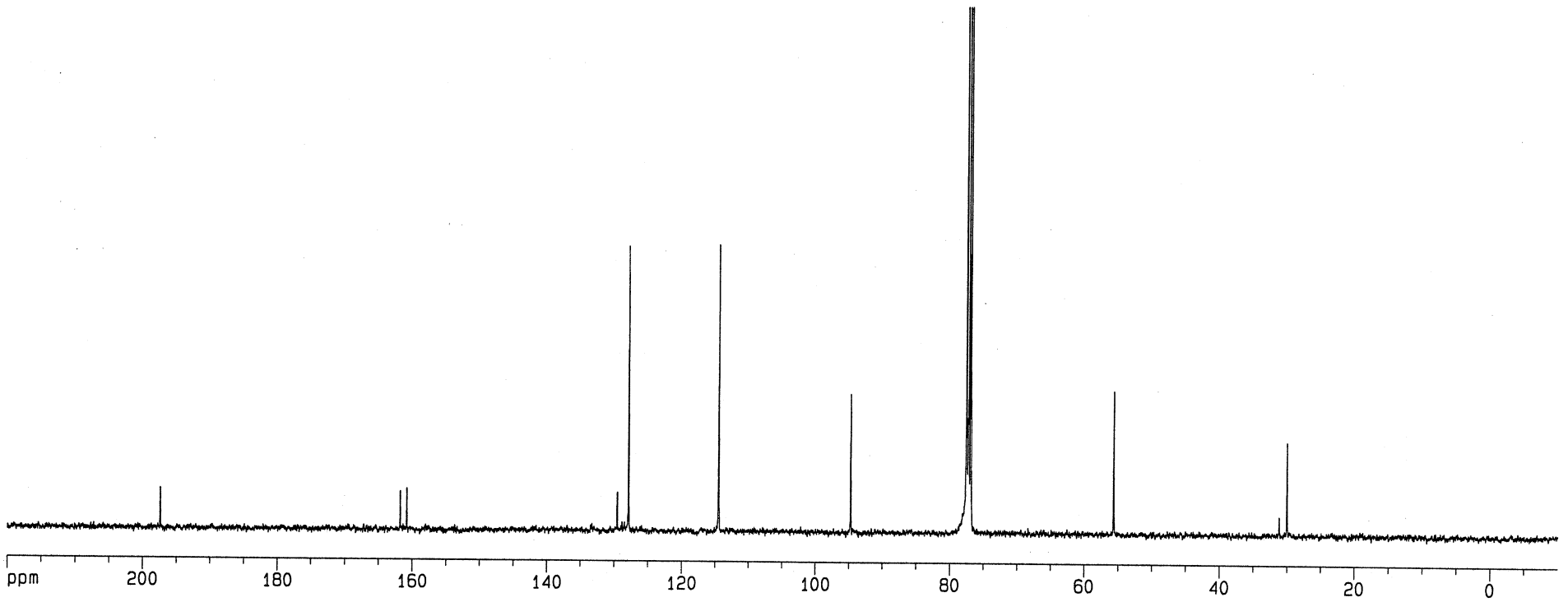
Integral
1.979
1.865
0.798
0.884
2.207
2.000
1.010
ppm
10
9
8
7
6
5
4
3
2
1
0

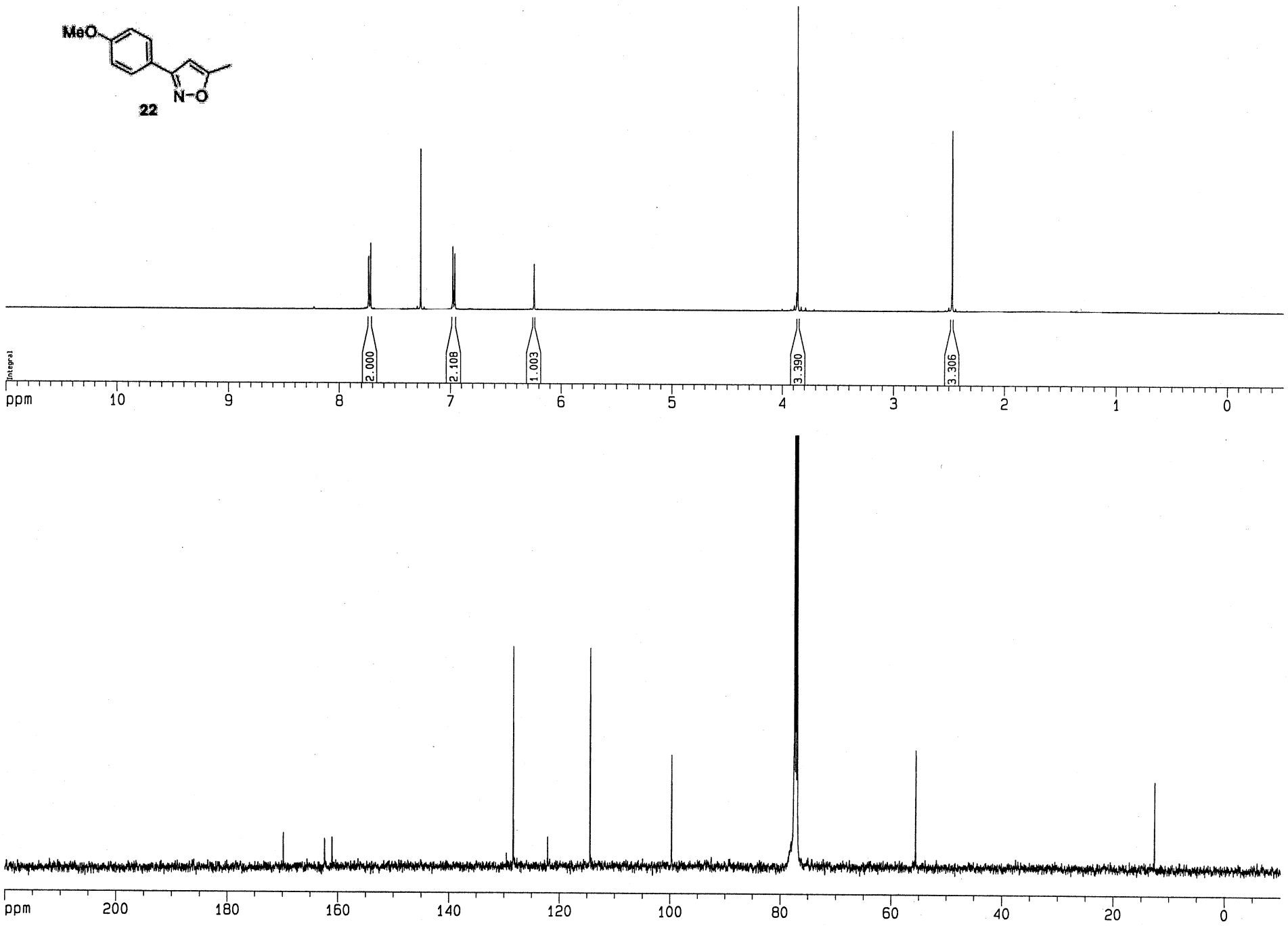

ppm
200
180
160
140
120
100
80
60
40
20
0

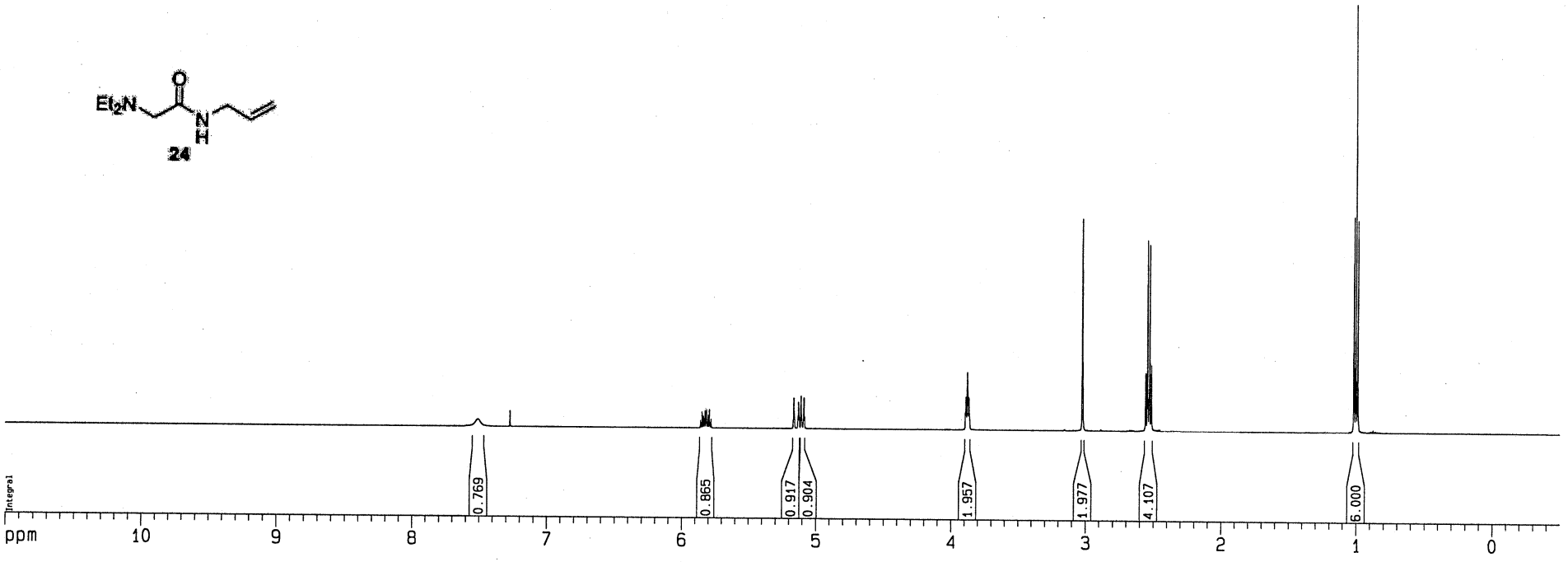

MeO
NH2
O

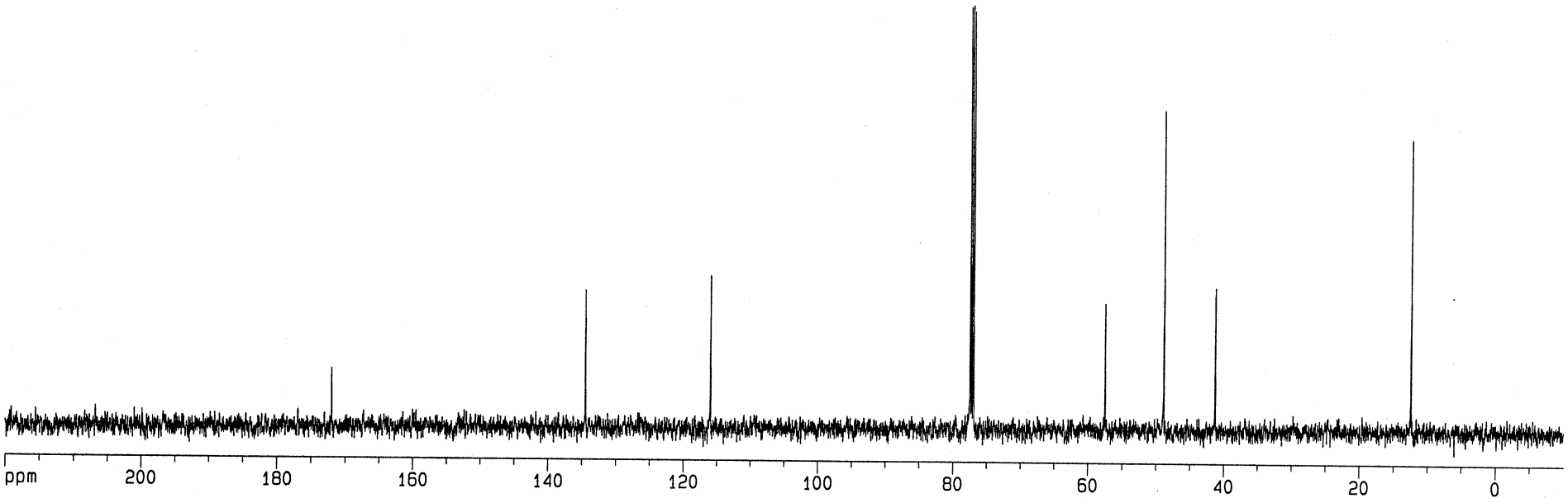
21

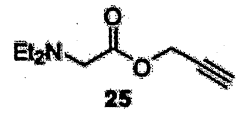
Integral
0.925
2.000
2.064
0.986
1.082
3.035
3.071
ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
N
O
22
Integral
2.000
2.108
1.003
3.390
3.306
ppm
10
9
8
7
6
5
4
3
2
1
0
ppm
200
180
160
140
120
100
80
60
40
20
0

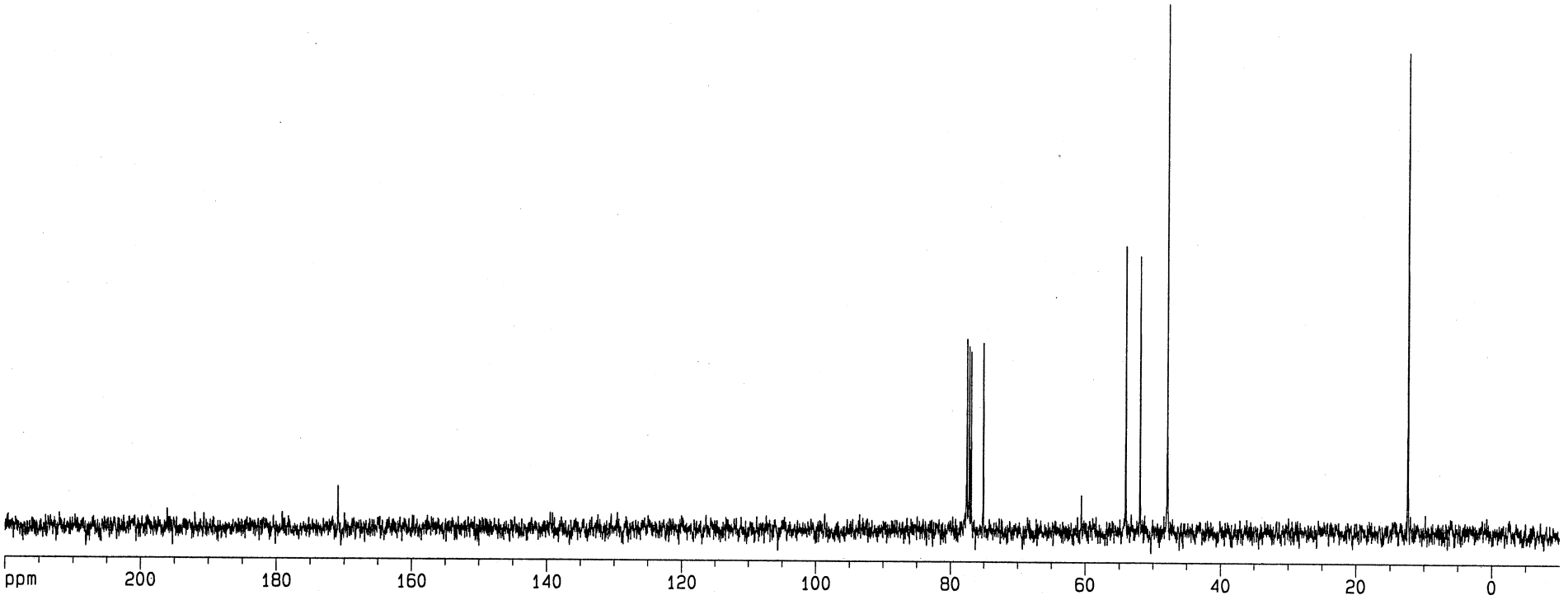

Et2N
O
N
H
24
Integral
0.769
0.865
0.917
0.904
1.957
1.977
4.107
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

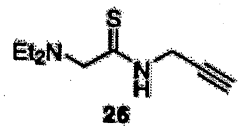

ppm
200
180
160
140
120
100
80
60
40
20
0


Et2N
O
O

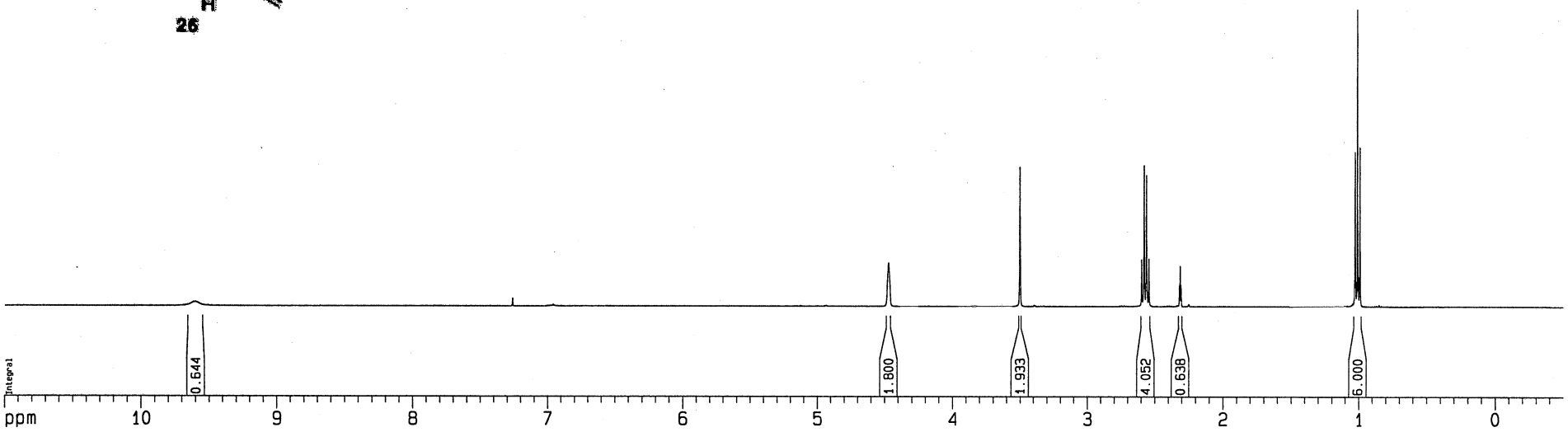
25

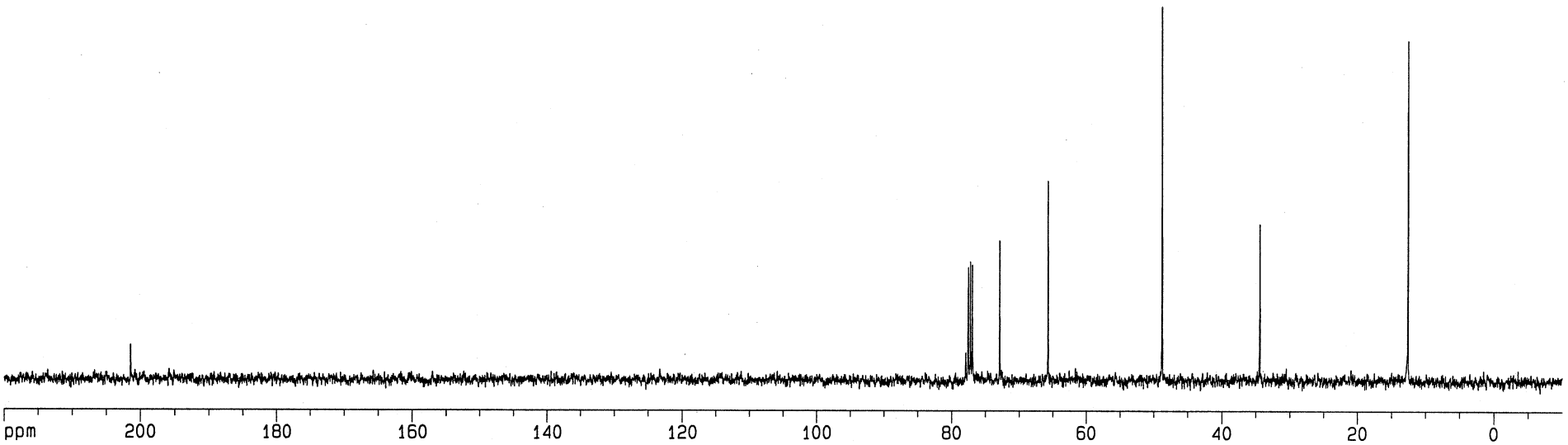
Integral
1.784
1.940
4.060
0.702
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

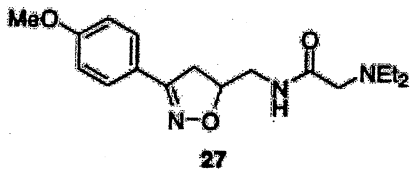

ppm
200
180
160
140
120
100
80
60
40
20
0


S
Et2N
N
H

26

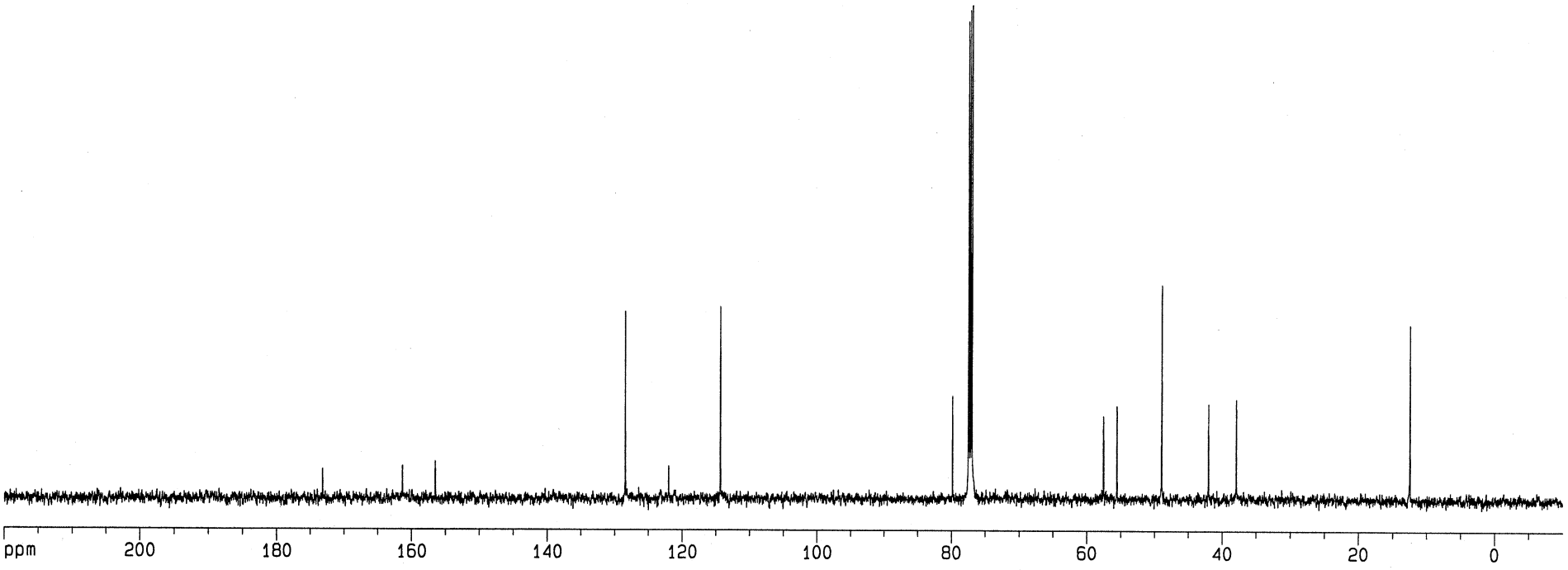

Integral
0.644
1.800
1.933
4.052
0.638
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

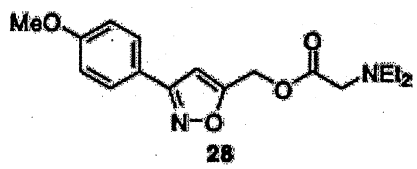

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
O
NEt2
N
O
H

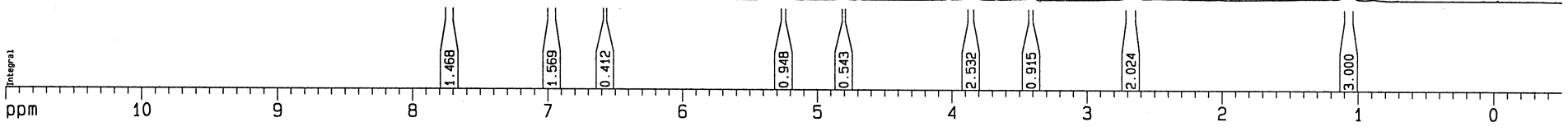
27

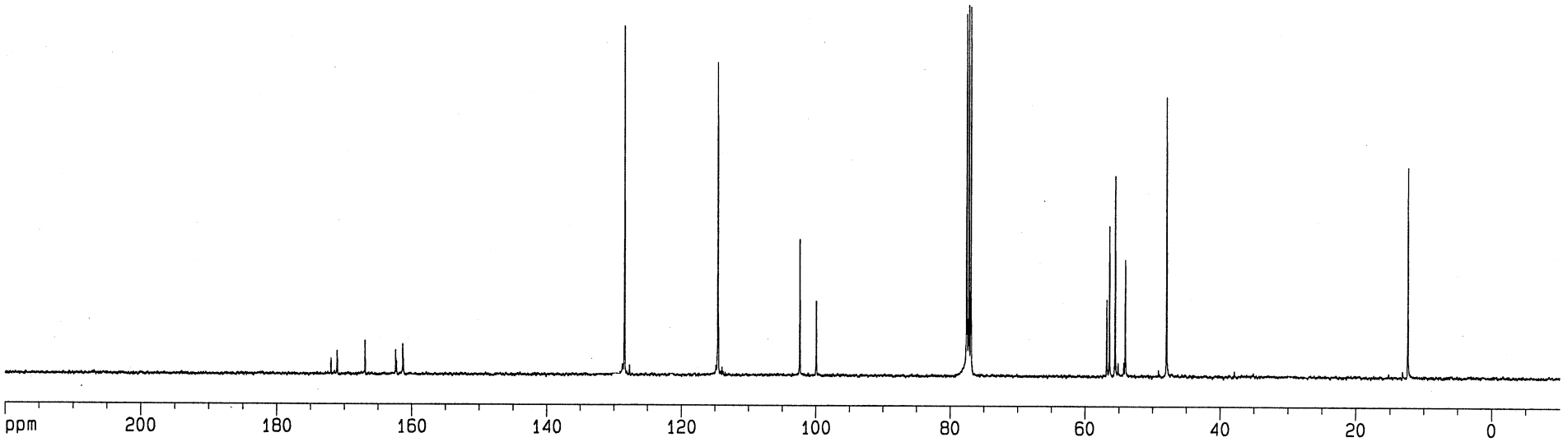
Integral
0.902
1.851
1.834
1.066
2.997
2.438
1.179
1.199
2.411
4.234
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0

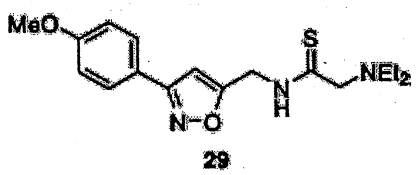

ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
O
NEt2
N
O
O

28

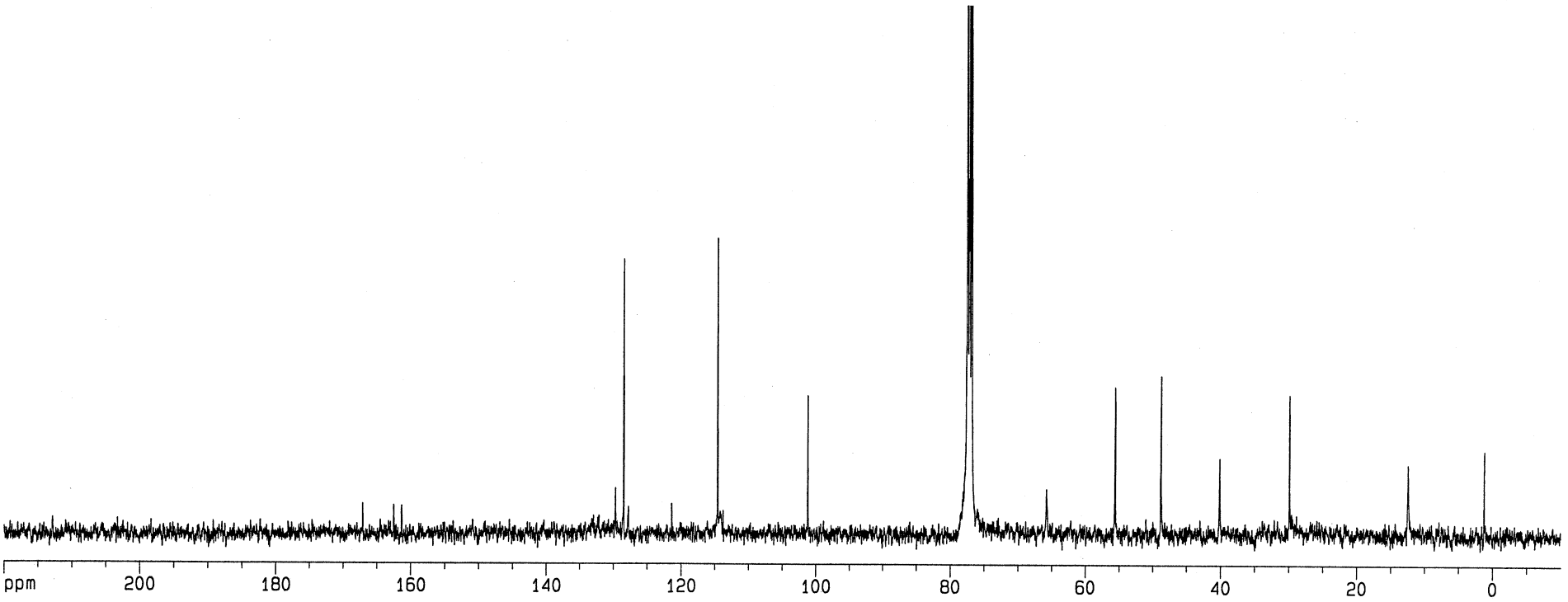

Integral
1.468
1.569
0.412
0.948
0.543
2.532
0.915
2.024
3.000
ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
200
180
160
140
120
100
80
60
40
20
0


MeO
S
NEt2
N
H
N–O

29

Integral
1.899
2.551
0.943
1.939
4.505
1.959
3.869
6.000
ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
200
180
160
140
120
100
80
60
40
20
0